

University of Dundee

MASTER OF DENTAL SCIENCE

Intra-Oral Three Dimensional Scanning for Assessment of Surgical Outcome in Patients with Unilateral Cleft Lip and Palate

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INTRA-ORAL THREE DIMENSIONAL SCANNING
FOR ASSESSMENT OF SURGICAL OUTCOME IN
PATIENTS WITH UNILATERAL CLEFT LIP AND
PALATE



A DISSERTATION PRESENTED FOR THE DEGREE OF MASTER
OF DENTAL SCIENCE

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LIST OF ABBREVIATIONS

ABO: American Board of Orthodontics

AFI: Accordion fringe interferometry

BCL: Bilateral cleft lip

BCLP: Bilateral cleft lip and palate

CAD/CAM: Computer-aided
design/computer aided manufacturing

CBCT: Cone beam computerised
tomography

CP: Cleft palate.

CL: Cleft Lip

CLEFTSiS: Cleft Services in Scotland

CLAPA: Cleft Lip and Palate Association

CLP: Cleft lip with or without cleft palate

CSAG: The Clinical Standards Advisory
Group

DNA: Deoxyribonucleic acid

EPG: Electropalatography

GBD: Global Burden of Disease

GWA: Genome-wide association study

ICON: Index of Complexity Outcome and
Need

IOTN: Index of Orthodontic Treatment
Need

I.U: Intrauterine

LED: Light emitting diode

MCN: Managed Clinical Network

MHB: Modified Huddart Bodenham

GOSLON: Great Ormond Street, London
and Oslo

HRQoL: Health Related Quality of Life

OFC: Orofacial Cleft

OJ: Overjet

PAR: Peer Assessment Rating

SES: Socioeconomic status

SNP: Single nucleotide polymorphism

UCLP: Unilateral Cleft Lip and Palate

VPI: Velopharyngeal insufficiency

WHO: World Health Organisation

2D: Two Dimensional

3D: Three Dimensional

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DECLARATION

This thesis is the original work of the author.

Unless stated, all references cited have been consulted by the author.

Work, of which this thesis is a record, has been done by the author.

This work has not been previously accepted for a higher degree.

Signed:

Date:

ABSTRACT

Background: Cleft lip and palate is the most common congenital craniofacial anomaly.

Orofacial clefting (OFC) presents as a heterogeneous group of disorders affecting the lips and oral cavity. Treatment involves a multidisciplinary team working with a high burden of care.

Evidence is lacking regarding the optimum timing of lip and palate repair. Audit records are part of clinical governance, collected to monitor quality of care, but they can also be used for research purposes to generate an evidence base for best treatment protocol. Surgical outcome indices can be scored from audit records. The World Health Organisation (WHO) recommends study models to be taken pre-surgery and at 5, 10 and 18 years of age. The impression-taking process can be upsetting to the child and result in a failure to comply (Clark et al., 2007).

Plaster study models can be scanned to create indirect three dimensional (3D) digital models and dental arches can be scanned directly using an intra-oral 3D scanner. The latter technique eliminates the need for impression taking but has not previously been investigated in cleft care.

Aims: This prospective study aimed to examine the reliability of intra-oral 3D scans as an alternative to study models in assessment of dental arch relationships in a sample of 5-21 year olds with unilateral cleft lip and palate (UCLP).

A secondary aim was to obtain patient and parent/carer feedback regarding acceptability of dental impressions and intra-oral 3D scans.

Hypotheses (null): There is no difference in the reliability of scoring dental arch relationships using the GOSLON and MHB indices on plaster and digital 3D study models.

There is no difference in patient / carer acceptability of routine dental impressions and intra-oral 3D scanning.

Materials and Methods: Forty-six patients with UCLP attended the data collection clinic.

Three patients withdrew as they did not wish to have routine dental impressions taken therefore 43 underwent routine dental impressions and intra-oral scanning [Trios® Digital Impressions Scanner € (3Shape A/S, Copenhagen, Denmark)] of their dental arches. Once cast the plaster models were scanned by an orthodontic 3D model scanner [R700 Orthodontic Study Model Scanner€ (3Shape A/S, Copenhagen, Denmark)] to create indirect digital study models. Three examiners scored the plaster, direct and indirect study models using the Great Ormond Street, London and Oslo, Norway (GOSLON) Yardstick and modified Huddart Bodenham (MHB) indices on 2 occasions, one month apart. All 43 participants and 32 accompanying parents/carers completed a simple questionnaire regarding the acceptability of the dental impressions and intra-oral scans.

Cronbach's Alpha was used to determine reliability scoring for each study model medium using the GOSLON scores. Inter-examiner reliability was assessed using Bland Altman plots for the MHB data with the data being tested for each model medium using a one-sample T-test ($P < 0.05$). The questionnaire data was statistically tested using Wilcoxon signed ranks tests ($p < 0.05$).

Results: All examiners and mediums of study models achieved an intra-examiner reliability score greater than 0.987, deemed to be above the acceptable range. The direct digital scans

demonstrated superior inter-examiner reliability to indirect digital and plaster models but differences were not statistically significantly different ($p>0.05$).

Feedback from the questionnaire indicated that participants strongly preferred the 3D scan ($p=0.00018$). There was no significant difference in regards their perception of the time required ($p>0.05$). The parents/carers preferred their child's experiences of the 3D scanner compared to the routine impressions ($p=0.003$) and the perceived time required ($p=0.030$).

Conclusions:

1. Reliability of GOSLON and MHB scoring using intra-oral three dimensional (3D) scans was superior to both plaster and indirect 3D digital models.
2. Subjects with UCLP and their parent/carer preferred the experience of the intra-oral 3D scan in comparison to routine dental impressions.
3. This study supports the replacement of conventional impressions with intra-oral 3D scans in longitudinal evaluations of the outcomes of cleft care.

CHAPTER ONE: INTRODUCTION

Clefting of the orofacial structures is the most common craniofacial anomaly caused by non-union of the facial and oral structures during the embryonic period. The prevalence of orofacial clefting (OFC) varies across the world and effects on average 1.7 per 1000 live births (Mossey *et al.*, 2009). Locally in Scotland a rate of 1.46 per 1000 live births (Clark *et al.*, 2003). The aetiology is thought to have both genetic and environmental contributions.

Persons born with OFC are burdened with the impact of clefting on their health and wellbeing. Speech, hearing, feeding, psychological problems and dental anomalies are commonplace in this patient group. Treatment of all presentations of cleft lip and palate requires a multidisciplinary approach. There is a wide diversity in models of cleft care, national policies and clinical practices across Europe (Shaw *et al.*, 1992). The quality of outcome of surgical repair of cleft lip and palate varies considerably. Evidence is lacking regarding the optimum timing of lip and palate repair.

As part of the process of generating an evidence base for the best treatment protocols i.e. optimising the quality of care for patients born with cleft lip and palate, it is important to monitor treatment outcomes and to carry out inter-centre comparison of outcomes. Part of the process of outcome assessment involves examining the effects of primary surgical repair on the dimensions of the maxillary (upper) arch form i.e. the extent of constriction of the upper teeth and the resultant occlusion as an indicator of surgical iatrogenesis. The World Health Organisation recommends that study models are taken for patients with complete cleft lip and palate (bilateral and unilateral) as a minimum records prior to primary surgery and at 5, 10 and 18 years of age (WHO 2000).

Current practice is that dental arch forms are recorded by producing plaster dental study models, which involves impression taking, which can be uncomfortable and unpleasant for some patients. The impressions are cast in plaster in a dental laboratory to create study models. There are several problems associated with study models mainly storage, breakage, loss (McGuinness and Stephens, 1992) and difficulty with inter-centre comparisons due to their bulk. Poor patient cooperation has been shown to be a common problem with taking impressions for study models in 5 year old patients with unilateral cleft lip and palate. Even though impression-taking is considered a less invasive procedure in comparison to other records taken at audit clinics, the process can be upsetting to the child (Clark *et al.*, 2007).

Technology developed in the 1990s (Fleming *et al.*, 2011) and subsequent software refinements have allowed indirect digital study models to be created by scanning plaster study models. Current applications allow linear measurements, treatment planning, Peer Assessment Rating (PAR) scoring, tooth size and space analysis. Digital models have been shown to be as accurate, reproducible and suitable for diagnosis and treatment planning within all fields of dentistry (Asquith *et al.*, 2007, Dalstra and Melsen, 2009, Fleming *et al.*, 2011).

More recently the technology has been developed to scan the dental arches intra-orally, creating direct digital study models, eliminating the requirement for impression taking and casting of traditional plaster study models. This has not been used as yet for cleft care.

Several classification systems of dental arch relationships and therefore surgical outcome have been described (Atack *et al.*, 1997a, Huddart and Bodenham, 1972, Mars *et al.*, 1987, Mossey *et al.*, 2003, Pruzansky and Aduss, 1964). The GOSLON (Great Ormond Street, London and Oslo, Norway) Yardstick (Mars *et al.*, 1987) and the modified

Huddart/Bodenham (MHB) (Mossey *et al.*, 2003) indices are commonly used (Altalibi *et al.*, 2013). Each are described in turn.

The GOSLON Yardstick uses five ordinal categories of treatment outcome, excellent, good, fair, poor and very poor, to score the patients occlusion and to predict the complexity of treatment required to correct the malocclusion. Only patients in the late mixed or early permanent dentition with unilateral cleft lip and palate can be scored using this index.

Assessors wishing to use the GOSLON Yardstick are required to undertake calibration training and reference models are a prerequisite.

The MHB index can be applied to study models of patients with clefts of the lip and palate in any subgroup at any age (Mossey *et al.*, 2003, Tothill and Mossey, 2007). The system uses the frequency of crossbites in the dental occlusion to evaluate relative maxillary arch constriction. Each tooth is awarded a score depending on its position relative to its opponent in the lower arch and a total score is obtained. The more negative the score, the more severe the arch constriction. The measurements used in the MHB scoring index lend themselves to calculations based on the assessment of digital images. Calibration training and reference models are not required (Dobbyn *et al.*, 2012).

Attempts have been made to remove the requirement for storing hard copy dental study models and allowing images of them to be transferred digitally. The GOSLON yardstick and MHB indices have been shown to be reliable when used to score photographic images of study models of subjects with unilateral cleft lip and palate (Ali *et al.*, 2006, Nollet *et al.*, 2004). More recently both indices have also been successfully used to score indirect 3D scans of plaster study models (Asquith and McIntyre 2012, Dogan *et al.*, 2012, Nicholls *et al.*, 2014, Servet *et al.*, 2012). The next progression is to eliminate the requirement for taking

dental impressions by capturing the dental arches digitally with a scanning system. The ideal system would have a short scanning time, be non-ionising, comfortable and have accompanying software with an algorithm for scoring the occlusion and maxillary arch construction.

This study investigates direct intra-oral scanning of the teeth for scoring surgical outcome measure in patients with UCLP ages 5-21. If this produces an accurate and valid recording of the occlusion it may be possible to avoid taking impressions for the purposes of outcome measurement (for audit and clinical governance) in the future. The routine plaster study models created from dental impressions will also be scored and a comparison made to the digital scans of the plaster models and direct intra-oral 3D scan models.

CHAPTER TWO: LITERATURE REVIEW

2.1 Aetiology and Pathogenesis of Orofacial Clefting

Clefting of the lip and palate occurs when the craniofacial structures fail to fuse. Clefts of the lip can present unilaterally (80%) or bilaterally (20%) (Cobourne 2012) and are classified as cleft lip with or without cleft palate or isolated cleft palate (Figure 1).

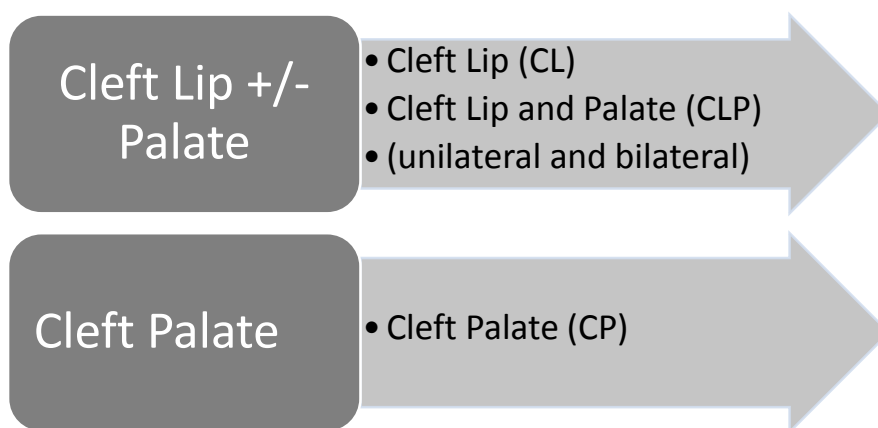


Figure 1 Classification of orofacial clefting. Adapted from Kernahan and Stark (1958).

2.1.1 Normal Development of the Face

The normal development of the peri-oral structures will be described to emphasise the complexity and coordination of events that occur within the embryonic stage [2-8 weeks *in utero* (i.u.)]. If these events do not occur at the right time and place, clefting may result.

The primitive mouth or stomodeum becomes open to the amniotic cavity at the end of the 3rd week i.u. when the cephalic end of the foregut membrane ruptures.

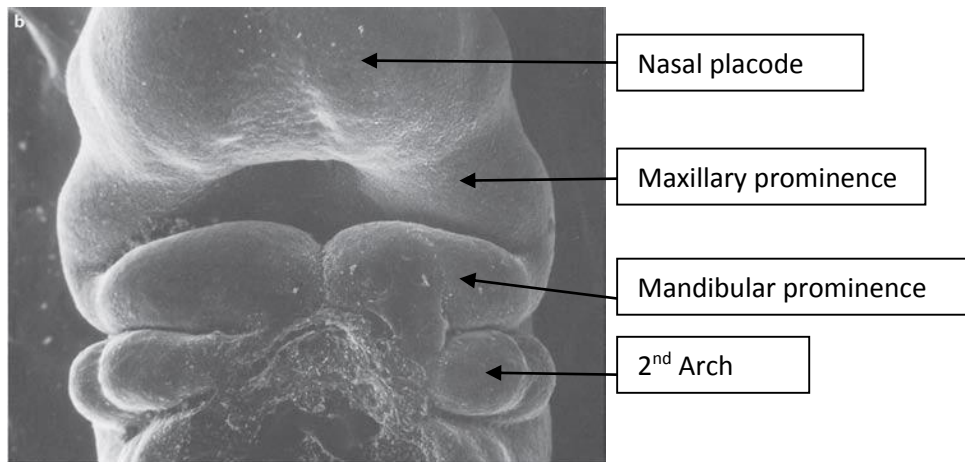


Figure 2 Scanning electron microscope of a human embryo aged 4.5 weeks. Adapted from (Sadler and Langman 2012)

The single frontal prominence borders the mouth opening rostrally in the midline and the nasal and optic placodes develop bilaterally within the surface ectoderm. During the 4th week i.u. following the migration of neural crest cells mesodermal prominences form around the stomodeum. These are derived from the first pharyngeal arch. The maxillary and mandibular processes are paired with the former located lateral to the stomodeum and the latter located caudal to this structure (Figure 2).

The mandibular processes grow towards each other and merge in the midline during the 6th week i.u. to form the lower lip. The maxillary processes also increase in size at this stage and grow medially but remain separated from the nose by a groove which later forms the nasolacrimal duct. A depression forms within each of the nasal placodes forming a pit dividing the edges of the forming nasal process into lateral and medial portions. The pits are separated in the midline by the nasal septum.

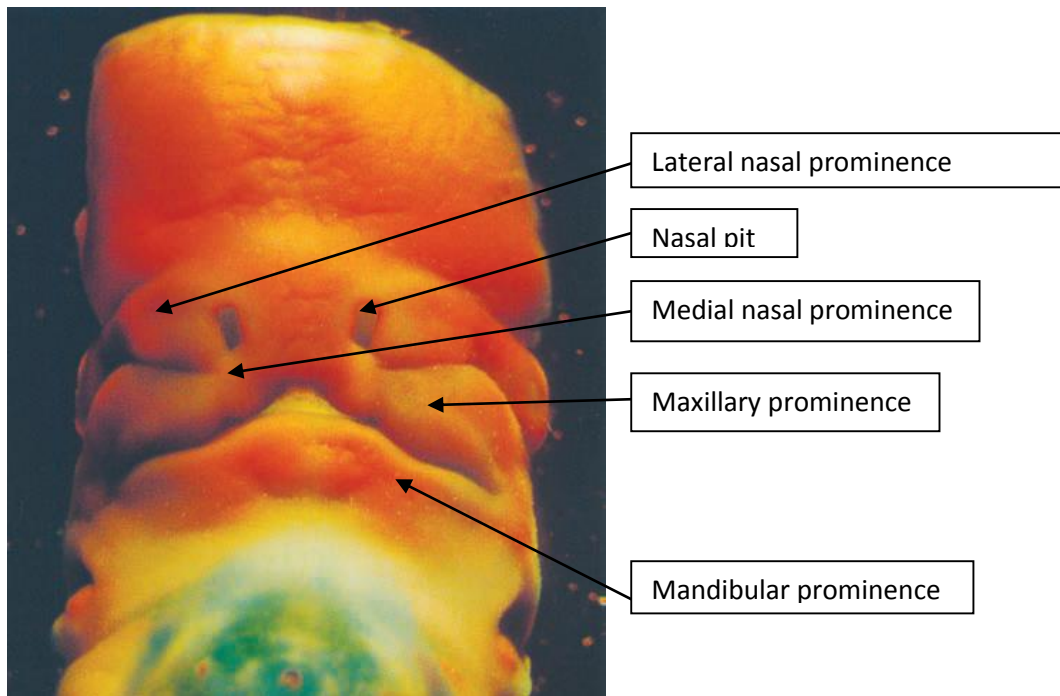


Figure 3 Photograph of a human embryo aged 7 weeks. Adapted from (Sadler and Langman 2012)

From week 7-10 i.u. the upper lip is formed by the combination of the bilateral medial nasal and the 2 maxillary prominences to create the intermaxillary segment (Figure 3). This structure has 3 components:

1. Labial – forms the philtrum of the upper lip.
2. Primary Palate – the triangular shaped portion of the anterior palate.
3. Median portion of maxilla – the area in which the upper incisors will develop.

2.1.2 Formation of the Secondary Palate

The palate is composed of two major parts, the primary palate and secondary palate (Johnson and Moore, 1997) . Prior to the formation of the secondary or definitive palate the tongue occupies the oronasal cavity.

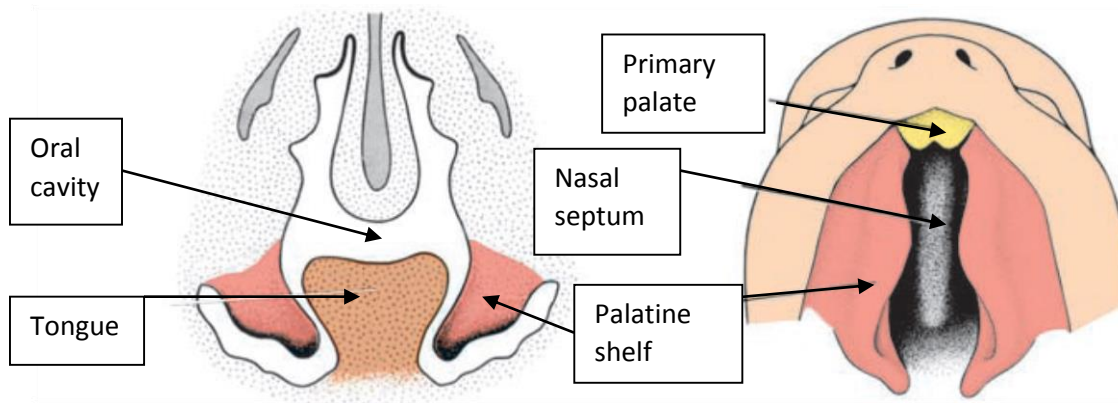


Figure 4 Left: Frontal section through the head of a 6.5-week embryo. Right: Ventral view of the palatine shelves after removal of the lower jaw and the tongue. Adapted from Sadler and Langman (2012)

During the 6-7th week i.u. mesenchymal extensions, derived from the neural crest, grow from the maxilla and are orientated vertically adjacent to the tongue (Figure 4). “Two peaks of cell division occur as the palatal shelves are formed: during initial shelf outgrowth and during vertical shelf elongation” (Berkovitz *et al.*, 2009). This occurs 1 week later in females. The palatine shelves are able to rapidly position themselves horizontally when the primitive mouth enlarges and the tongue moves downward during the 8th week i.u. (Figure 5). The shelves are thought to elevate within a matter of minutes or hours (Ferguson 1988). The paired shelves fuse and have mesenchymal continuity with each other in the midline, the primary palate anteriorly and the inferior margin of the nasal septum (Figure 6).

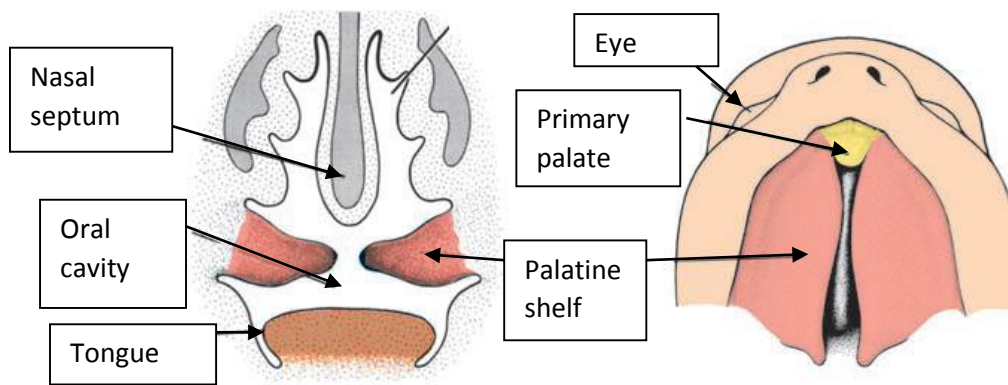


Figure 5. Left: A frontal section through a 7.5 week old embryo. Right: Ventral view of the palatine shelves after removal of the lower jaw and the tongue. Adapted from Sadler and Langman (2012)

The incisive foramen marks the transition from the primary to secondary palate anatomically in the midline. Extrinsic factors are thought to influence the lifting of the shelves. These include increased facial height, lifting of the head, movement of the tongue and differential pressures around the shelves. Intrinsic factors within the mesenchyme have also been proposed. Hyaluronan within the extracellular matrix of the palatal tissue is thought to play an important role in elevation. This glycosaminoglycan is electrostatically powerful at producing turgor pressure as it is able to bind to water several times its own weight (Ferguson 1988). Statistically significantly increased levels of hyaluronan have been found in the palatal tissues of rats pre-elevation when compared to post-elevation although no difference exists between the anterior and posterior palate (Singh *et al.*, 1994). Hyaluronan is also thought to influence cell growth and differentiation which is key as it is thought that a critical number of mesenchymal cells are essential for palatogenesis. Type 1 collagen is found vertically in bundles within the shelves and any erecting force they produce may be directed by these fibres (Ferguson 1988).

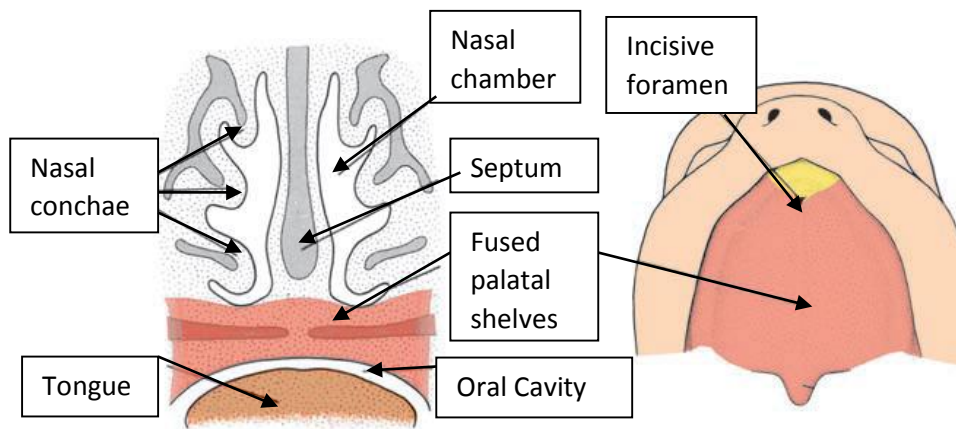


Figure 6. Left: A frontal section through a 7.5 week old embryo. Right: Ventral view of the palatine shelves after removal of the lower jaw and the tongue. Adapted from Sadler and Langman (2012)

When the shelves first meet in the middle third of the palate, they join with a 'sticky' glycoprotein contact. An epithelial seam is created by the development of desmosomes which are programmed to only link with palatal tissue to prevent adhesion to other tissues such as the tongue (Berkovitz *et al.*, 2009). To allow the secondary palate to become continuous, the covering epithelial seam must break down. 'To achieve this fusion, DNA synthesis ceases within the epithelium some 24 to 36 hours before epithelial contact' (Nanci and Ten Cate, 2003). The mechanism by which this occurs is a topic of debate, with suggested methods including:

- Programmed cell death – 'apoptosis'
- Epithelial-mesenchymal transformation – cells assume fibroblast-like features (Nanci and Ten Cate, 2003)

2.2 Environmental Aetiological Factors

Non-syndromic orofacial clefts have a multifactorial aetiology, involving both genetic and environmental factors (Mangold *et al.*, 2011). These factors are thought to have a role in the disruption of the coordination of facial development creating a cleft. Lifestyle and environmental risk factors are important in clefting and maternal exposure to tobacco smoke, alcohol, poor nutrition, viral infection, medication and teratogens have been the subjects of considerable previous research (Figure 7) (Mossey *et al.*, 2009).

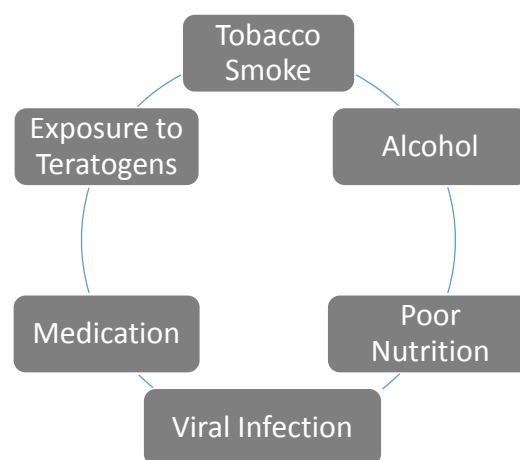


Figure 7 Lifestyle and environmental risk factors.

2.2.1 Tobacco smoke

Maternal tobacco smoking

There have been many public campaigns to inform expectant mothers about the dangers of smoking to their unborn children with the risk of low birth weights and breathing problems previously having been highlighted. Tobacco smoking is the most studied environmental risk factor in cleft lip and palate (Wyszynski and Wu, 2002). Smoking during pregnancy has been shown to have a moderate positive association with clefting, increasing the risk of having a baby with CL+/- P by 30% and CP by 20% (Chevrier *et al.*, 2005, Little *et al.*, 2004).

An association between maternal smoking and orofacial clefting was found to be close to null by (Wyszynski and Wu, 2002) but they discovered a trend between increasing levels of smoking and the risk of clefting. Pooling of the results using a similar method (Chung *et al.*, 2000) produced a dose-response analysis that was slightly significant.

Passive tobacco smoke exposure

A case-control study carried out in the United States of America did not find an association with environmental tobacco smoke exposure with clefting (Honein *et al.*, 2007). Furthermore, no association was found between passive smoking by the partner and oral cleft in a similar prospective Danish study (Bille *et al.*, 2007). However, a more recent Chinese study has implicated passive tobacco smoke exposure during the first trimester in infants with a specific genotype synergistically increasing the risk of clefting (Li *et al.*, 2011).

2.2.2 Alcohol Consumption

The consumption of alcohol during pregnancy is not uncommon and has known consequences such as foetal alcohol syndrome but other effects, such as clefting, are less well defined (Pruett *et al.*, 2013).

Potential genes linked to clefting that may interact and become modified by the metabolism of ethanol and other alcohols are transforming growth factor alpha (TGFA), transforming growth factor beta 3 (TGFB3), and Msh homeobox homolog 1 (MSX1) (Romitti *et al.*, 1999).

Several studies have found evidence in support of an association between consumption of alcohol during pregnancy and non-syndromic clefting (Bille *et al.*, 2007, Chevrier *et al.*, 2005, Romitti *et al.*, 1999). The risk according to the amount of alcohol consumed is controversial with some research finding heavy or 'binge drinking' (Shaw and Lammer, 1999) to be causative, whereas others have found more moderate levels to have an effect (Chevrier *et al.*, 2005, Meyer *et al.*, 2003, Romitti *et al.*, 1999) or no affect at all (Meyer *et al.*, 2003). The type of alcohol ingested may also have its own

risk as different beverages have varying concentrations of ethanol. Romitti *et al.*, (2007), found that the odds ratios differed by the type of alcohol consumed, particularly for cleft palate (distilled spirits > wine > beer).

Alcohol may act alone as a risk factor but other factors may affect a pregnant mother and impact synergistically increasing the risk of cleft (Shaw and Lammer, 1999).

2.2.3 Nutrition

It is very challenging to assess the nutritional profile and dietary intake of a study population. Folate, a water soluble B vitamin and its synthetic oxidised form folic acid have drawn much attention over their abilities to help prevent neural tube defects when taken pre-conceptually. B vitamins are essential for the synthesis and repair of DNA, cell division and red blood cell production. Folic acid is not synthesized by the human body and has to be supplemented or consumed in foodstuffs. Daily supplements of folic acid are recommended by government health departments across the world (Botto *et al.*, 2006).

A protective role of folic acid has been suggested by a number of intervention studies on the recurrence of oral clefts (Johnson and Little 2008). In the United States of America where some food is fortified with folic acid, a reduction in clefting has been found (Botto *et al.*, 2006).

Another B vitamin deficiency, vitamin B-6 has been implicated in orofacial clefting. Low maternal levels of B-6 are found across Asia where polished rice is a dietary mainstay. This type of rice loses a high proportion of its nutritional content during its processing. The risk of clefting in areas of the Philippines where maternal vitamin B-6 levels are high was found to be significant and dose related (Munger *et al.*, 2004).

Many studies investigating the relationship between vitamin intake and clefting have investigated pregnant mothers who have taken multivitamins including folic acid making it difficult to determine which component of the supplement had the precise clinical effect. Also the taking of multivitamin

supplements is a positive health lifestyle practice which may correlate with other recommended behaviours such as abstaining from consuming alcohol or smoking while expecting. This is likely to result in confounding. It has been shown that planned pregnancies are at a lower risk of producing a child with a cleft potentially allowing mothers to be to implement good health practices prior to conception (Mossey *et al.*, 2007).

2.2.4 Viral Infection

Influenza is a viral infection and commonly presents with a raised body temperature and can occur during pregnancy.

An association between influenza during the second and third month of pregnancy and cleft lip and palate has been shown and a weaker association with cleft palate (Acs *et al.*, 2005). The same study showed the adverse effects on the developing foetus can be reduced by administering anti-fever drugs. Acs *et al.*, (2005) concluded that the pyrexia was more likely to have caused the teratogenic effects than the virus, as an association was not seen in mothers who had received treatment for their hyperthermia. High temperature may result in the arrest of mitotic activity and immediate death of cells in mitosis with threshold elevations (1.5-2.5°C) and delayed death of cells in the S-phase (synthetic phase of DNA replication) with higher elevations (3.5°C) (Metneki *et al.*, 2005).

Influenza vaccination and immediate administration of anti-pyrexial medication is recommended for pregnant women (Acs *et al.*, 2005, Metneki *et al.*, 2005). It should be noted that all women at any stage of pregnancy in the United Kingdom are recommended to have an influenza vaccine (NHS, 2013).

2.2.5 Medication

Medication taken by pregnant mothers can have a potentially teratogenic effect, with drugs for the treatment of epilepsy being one of the most common. First generation antiepileptic such as phenytoin and carbamazepine had several side effects. Newer second generation drugs including

lamotrigine and topiramate are being prescribed to women as their molecular design is less 'interacting' but still pose a risk to the development of cleft lip and palate (Holmes and Hernandez-Diaz 2012).

Corticosteroids are prescribed routinely for a wide variety of conditions and can cross the placenta in pregnancy. A meta-analysis found there to be a threefold increased risk of oral clefting on exposure to corticosteroid in the first trimester (Park-Wyllie *et al.*, 2000).

2.2.6 Occupational Exposures

Human beings can be exposed to chemicals occupationally e.g. through the use of pesticides. Oral clefts have been found to have an increased risks for exposed individuals in some studies (Garcia 1998). A case-control study carried out in California found that a wide variety of chemicals can be encountered occupationally but did not find any that contributed significantly to the risk of clefting. The authors highlighted the need for further studies performed on a larger scale as chemical exposures are infrequent (Shaw *et al.*, 2003). Organic solvents were not found to be strongly associated with orofacial clefting in another case control study (Desrosiers *et al.*, 2012).

2.3 Genetic Aetiological Factors

OFC occurs as a non-syndromic event or present as part of a syndrome and with other congenital abnormalities. Cleft lip with or without palate presents as an isolated anomaly in 70.8% of cases and 29.2% are associated with other defects (Calzolari *et al.*, 2007). There are over 300 syndromes associated with clefting, examples include Pierre Robin sequence, Van der Woude, Velocardiofacial and Treacher Collins syndromes. A higher proportion of syndromic clefts involve CP (25%) compared to CL/P (12%) (Cobourne 2012). Congenital malformations can include musculoskeletal abnormalities such as limb reductions and polydactyly, cardiovascular complications with atrial and ventricular septal defects and central nervous system defects which may result in a cognitive dysfunction.

'It is generally accepted that CL/P and CPO are genetically distinct phenotypes in terms of their inheritance patterns' (Lidral *et al.*, 2008). A family history is reported in 40% of cases with CLP (Figure 8) but this strong familial clustering has not revealed consistent evidence for any single mode of inheritance for nonsyndromic CL/P (Zeiger *et al.*, 2003). A concordance rate of only 40 to 60% in monozygotic twins indicates that genetics alone are not responsible and previously mentioned environmental factors play an important etiological role in CLP (Lidral *et al.*, 2008).

Genetic risks of cleft lip and palate:

- Parents with no cleft but one affected child: risk for next child = 1 in 25
- One parent with CL/P: risk for first child = 1 in 50
- One parent with CLP and first child with CL/P: risk for next child = 1 in 10
- Both parents affected: risk for first child = 3 in 5

Figure 8. Genetic risks of cleft lip and palate. Adapted from Mitchell *et al.*, (2013)

Research to gain an understanding of the genetic factors contributing to the aetiology of OFC is crucial for the potential for prevention and improved treatment and prognosis. Prior to 2009 only one gene, interferon regulatory factor 6 (IRF6) had been shown to be consistently identified as a

non-syndromic CLP associated gene (Mangold *et al.*, 2011). IRF6 has an association with van der Woude syndrome. A commonly analysed gene transforming growth factor alpha (TGFA) has shown association with CLP in some case-control studies but not in linkage studies (Zeiger *et al.*, 2003).

Linkage studies are often limited due to small numbers of affected families.

Genome-wide association studies (GWAS) allow common variants, single nucleotide polymorphisms (SNPs), to be compared between multiple patient groups with and without a condition. This tool has identified a locus on chromosome 8q24, 10q25 and 17q22 (Birnbaum *et al.*, 2009). A consistently identifiable causative gene has yet to be discovered (McIntyre 2014a). Proof of causality requires further research but the genome mapping front-line research will hopefully unlock further information regarding the complex aetiology of OFC.

2.4 Gene-environment Interactions

The interaction between environmental factors and genetic variations may increase the risk of OFC in an unborn child. Studies have looked at these relationships with smoking being the most frequently researched environmental factor (Murray 2002) (Figure 9). If causative interactions can be proven, appropriate risk modification advice can be given to mothers. Genetic counselling should be offered to families with more than one affected member with CLP (McIntyre 2014a).

Gene/Environmental
TGFA/Smoking
TGFA/Alcohol
TGFA/Vitamins
MSX1/Smoking
MSX1/Alcohol
TGFB3/Smoking
TGFB3/Alcohol
RARA/Smoking
MTHFR/Vitamins
P450/Smoking
GST/Smoking
EPHX1/Smoking

Figure 9 Gene–environment interactions in cleft lip and palate. Adapted from Murray (2002)

2.3 Epidemiology

Orofacial clefting is a common birth defect affecting approximately 1.7 per 1000 live births (Mossey *et al.*, 2009) and can vary with ethnicity and geographies. The prevalence of CP and CLP by Global Burden of Disease (GBD) Regions in can be seen in Table 1.

A population based study carried out in Scotland found the local rate of OFC to be 1.46 per 1000 live births (Clark *et al.*, 2003). A similar prevalence (1.47 per 1000 live births) has been found in Northern Ireland (Gregg *et al.*, 2008).

Levels of CLP have been found to be low in Israel, South Africa and southern Europe and CP rates are low in Latin America and South Africa. Regions with high rates of CLP include Latin America and Asia (China, Japan) and Canada and parts of northern Europe for CP (Mossey and Modell 2012). Migrants to Hawaii from Japan and China were studied and they showed levels of OFC in line with their home ethnicity rather than to their new country of residence (Ching and Chung, 1974).

The prevalence of OFC varies across the sexes and with cleft phenotype. CLP is more common in males and CP in females. Clark *et al* (2003) found the male to female ration of CLP in Scotland to be 1.8:1 and isolated CP 0.8:1. The male prevalence in CLP is more apparent with increasing severity of clefting (Mossey *et al.*, 2009). There is a 2:1 ratio of left to right sided clefts among unilateral cleft lip cases (Dixon *et al.*, 2011).

GBD Region	Total orofacial clefts /1,000 (non-chr)	CP /1,000 (non-chr)	CL(P) /1,000 (non-chr)	CP % of total
Latin America, Southern	2.39	0.72	1.67	30
Latin America, Tropical	2.39	0.72	1.67	30
Australasia	2.01	1.02	0.98	51
North America, High Income	2.00	0.83	1.17	41
Oceania	1.85	1.13	0.72	61
Europe, Western	1.66	0.59	1.07	35
Asia Pacific, High Income	1.65	0.64	1.00	39
Asia, South	1.60	0.30	1.30	19
Latin America, Central	1.54	0.39	1.15	25
Europe, Central	1.45	0.67	0.77	47
Asia Southeast	1.36	0.28	1.08	20
Latin America, Andean	1.29	0.17	1.12	13
Asia, East	1.28	0.27	1.01	21
Europe, Eastern	1.22	0.59	0.63	49
Asia, Central	1.19	0.62	0.57	52
Middle East	1.02	0.30	0.72	29
Caribbean	0.93	0.31	0.62	34
Sub-Saharan Africa, Central	0.54	0.04	0.51	7
Sub-Saharan Africa, West	0.54	0.08	0.46	15
Sub-Saharan Africa, Southern	0.45	0.15	0.30	33
North Africa	0.44	0.15	0.29	35
Sub-Saharan Africa, East	0.38	0.12	0.27	31
WORLD	1.25	0.31	0.94	25

Table 1 Estimated birth prevalence of orofacial clefts by GBD region: ranked in descending order of prevalence. Adapted from Mossey and Modell (2012)

2.4 The Impact of Orofacial Clefting

When a child is born with OFC they, along with their family begin a journey with many challenges that will impact on their health and wellbeing (Figure 10). In the UK and several developed countries a multidisciplinary team is on hand to help them with the challenges that they will face.

The cleft team includes the following members:

- Surgeons: plastic, ear nose and throat, maxillofacial
- Paediatric dentists
- Orthodontists
- Cleft nurses
- Speech and Language therapists
- Geneticists
- Psychologists

National and International studies of cleft care have been undertaken to improve the care given to patients with OFC. In 1995 the Clinical Standards Advisory Group (CSAG) commissioned a national study of the current status of cleft care in the UK (Sandy *et al*., 1998). The results of this study were compared to an earlier European inter-centre study, 'Eurocleft' (Shaw *et al.*, 1992) which included 2 cleft units in the UK.

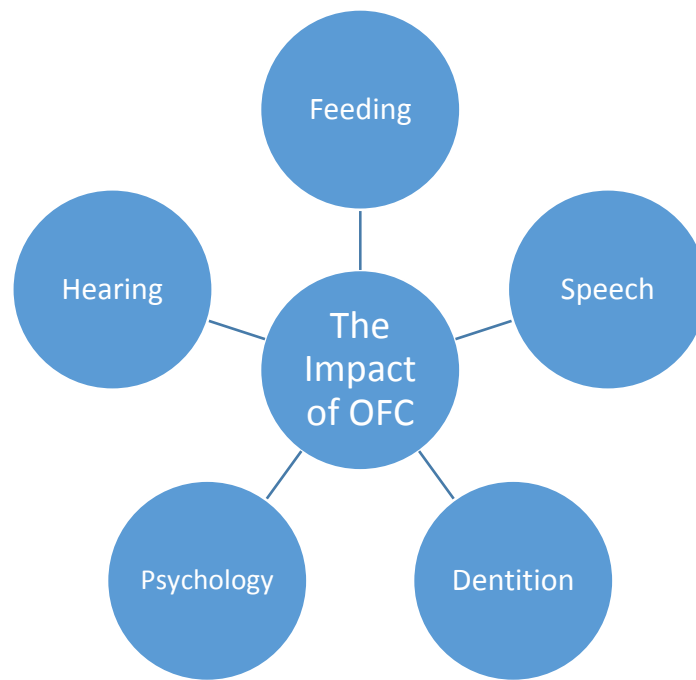


Figure 10 Impacting health and wellbeing impacts of OFC.

2.4.1 Feeding

Feeding problems are often the first obstacle experienced by a baby with a cleft. Feeding difficulties in clefts of the palate arise from a communication being present between the oral and nasal cavities. Suction by creating negative intraoral pressure is difficult to achieve causing the babies to experience nasal regurgitation, choking, prolonged feeds and discomfort (Reid 2004) and can lead to under nutrition and compromised growth.

Children with isolated CP have been found to be more likely to have feeding problems than those with CL or CLP. The majority of problems resolve following palate repair (Lee *et al.*, 1997). Mean neonatal weight gain has been noted to be lower in 25% of babies with clefts compared to the expected levels in non-cleft babies (Jones 1988).

The World Health Organisation strongly advocates breastfeeding for the first 6 months of life but this can prove to be very difficult for babies with clefts and their mothers. A recent

study carried out in the West of Scotland found breastfeeding rates to be lower in the cleft group in comparison to the general population and had diminished to half the level at six months postpartum. Significantly more infants with CLP than CL required assisted feeding support from a nasogastric tube (Britton *et al.*, 2011).

A variety of feeding bottles (Figure 11) are available to assist cleft babies including ones with compressible bottles and modified nipples (Reid 2004).



Figure 11a Haberman Feeder



Figure 11b NUK Cleft Palate Teat

2.4.2 Hearing

Palatal muscles control the opening of the Eustachian tubes of the ear. In normal function the tube is filled with air, if there are abnormalities of the placement of the tensor veli palatine and levator veli palatine muscles it can become filled with liquid and can cause hearing loss and middle ear infections (otitis media or 'glue ear').

Otitis media occurs more frequently (90%) in the first year of life in the CLP population in comparison to the general population (50%). Permanent conductive hearing loss is known to occur in 50% of the CLP population (Kuo *et al.*, 2013).

The placement of a small ventilation tube, commonly known as a grommet, into the ear drum prevents a build-up of fluid. This practice is recommended in the majority of patients with cleft (Conley 2014).

2.4.3 Speech

Hearing difficulties along with palatal fistulae and velopharyngeal dysfunction can lead to speech problems in a child with CLP. Velopharyngeal insufficiency is due to an inability of the soft palate to reach the pharyngeal wall. The lack of a seal allows air to escape between the oral and nasal cavities causing speech to sound hypernasal with difficulties pronouncing pressure consonants (Wyatt *et al.*, 1996).

The UK CSAG study found that just over a half of preschool age (5years) children and just under a fifth young adolescents (12 years) had poor speech outcomes and were categorised as different enough to provoke comment (Sell *et al.*, 2001). Speech has been seen to have a significant relationship with Health Related Quality of Life (HRQoL) with better speech relating to a higher score (Damiano *et al.*, 2007).

2.4.4 Psychology

OFC can affect individuals psychologically as well as physically. A survey of a sample of patients with clefts in the UK revealed that 73% 15-20 year olds felt that their cleft had affected their self-confidence and 60% had been teased about their speech or appearance (Turner *et al.*, 1997).

A study of adolescents with CLP in Sweden found that they were more likely to experience significant deficits in educational achievement. CP was found to have the most negative outcome followed by CLP then CL (Persson *et al.*, 2012). The study was not able to explain the differences between cleft groups and further research is required in this area.

Social functioning can be affected by OFC. When compared to controls, children with CLP have been suggested to have fewer friends than normal controls. Adults with CLP have been found to have lower marriage rates, marry later in life and have childless marriages (Hunt *et al.*, 2005).

A long term follow up study of individuals with CLP found an increased number of expected deaths with an increased mortality up until the age of 55. The risk of suicide in males and females with CLP was significantly increased (Christensen *et al.*, 2004).

2.4.5 Dentition

Teeth in the region of a cleft of the alveolus may be congenitally absent, have abnormal enamel or morphology. The general dentition in cleft patients have an increased prevalence of supernumerary teeth, hypodontia, microdontia and delayed eruption (Mitchell *et al.*, 2013).

Maxillary canine impaction is at an increased risk (20%) in alveolar clefts in comparison to the general population (2%). Secondary bone grafting of the alveolus aims to eliminate the residual cleft. The optimum timing of the surgery is aged 9-11 years prior to eruption of the maxillary canines, allowing them to erupt through the graft (Bergland *et al.*, 1986). Of the 157 children with UCLP in the CSAG study only 58% had a successful bone graft (Sandy *et al.*, 1998). This was in comparison to one of the centres included in the Eurocleft study who had a 97% success rate (Shaw *et al.*, 2001).

A systematic review of case-control studies found no firm evidence that there is an increased caries rate in children with CLP (Hasslof and Twetman 2007). The CSAG report found 40% of 5 year olds and 20% of 12 year olds with UCLP to need treatment for dental decay (Sandy *et al.*, 1998).

Orthodontic treatment is commonly required prior to bone grafting to expand any transverse collapse of the alveolus. When the patient is in the permanent dentition further orthodontic treatment is likely to be required. Around 25% of patients with CLP will require a joint orthodontic and orthognathic surgery treatment to correct their malocclusion (Mitchell *et al.*, 2013).

Reduced growth of the face and maxilla is common following surgical repair in CLP. The cause of the retrusion is not fully understood but is thought to be related to the restriction of growth due to scar tissue secondary to surgical repair (Mars and Houston, 1990). The CSAG study found 37% of 5 year olds and 39% of 12 years to have 'poor' or 'very poor' dental arch relationships (Sandy *et al.*, 1998). This was substantially higher than the dental arch relationships of the 12 year old patients with UCLP in the Eurocleft study (Bearn *et al.*, 2001). Several occlusal indices have been developed to score the dental arch relationships as surgical outcome measures and will be discussed in a subsequent chapter (2.7).

2.5 Health Inequalities

Inequalities in health exist both nationally and internationally. Due to deficiencies in record keeping in developing countries it is difficult to obtain a complete geographical picture of the distribution of clefts and associated care.

In developed countries, socioeconomic status (SES) can lead to health inequalities. Locally in Glasgow, Scotland an association between SES and OFC has been shown with the highest rates in the more deprived areas. The effect was greater for CP than for CLP (Clark *et al.*, 2003). A similar relationship was found in Wales by (Durning *et al.*, 2007). A case-control study carried out in California did not find an association with worse SES and with increased risk of OFC (Carmichael *et al.*, 2009).

In the UK and Europe national and international studies have helped improve cleft care service organisation (Sandy *et al.*, 1998, Shaw, *et al.*, 1992). This remains a problem in developing countries along with inequality of access to care, and treatment uncertainty (Mossey *et al.*, 2011). In India it is not uncommon for patients with CP to present in the second decade untreated (Ramana *et al.*, 2005). Late presentation is a reflection of access to care. The uppermost line depicted in Figure 12 shows the age/% survival relationship for the UK population. The middle curve shows a modestly increased all-cause mortality for patients with surgical correction of OFC during infancy. The inferior line shows data collected by the charity Smile Train in India from patients with untreated OFC who have a lower survival rate.

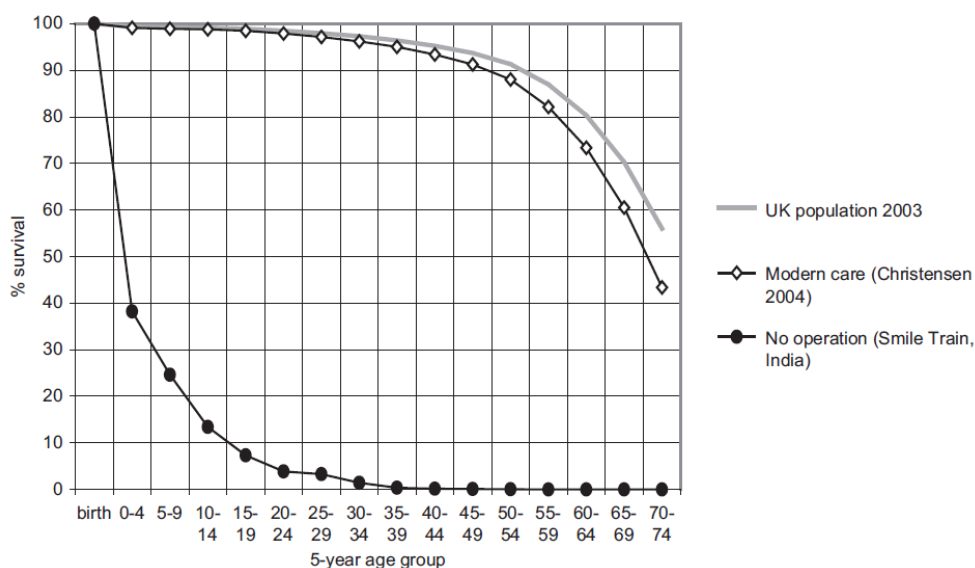


Figure 12 Access to care as indicated by age at primary surgery. Adapted from Mossey *et al.*, 2011). The upper curve shows long-term survival of patients with OFC repaired in infancy: there is modestly increased all-cause mortality at all ages. The lower curve shows estimated survival with unoperated OFC in India, based on Smile Train data

2.6 Cleft Care

A child born with a cleft has a high burden of care (Britton *et al.*, 2011) and specialist care continues from pre-natal to adulthood (Sandler *et al.*, 2014). Once diagnosed, the baby will be referred to their nearest Cleft Team. The multidisciplinary team of health professionals is outlined Figure 13 and, in addition input is also commonly sought from Geneticists, Paediatricians and Psychologists. As well as clinical care the Cleft Team are involved in service development, teaching, training, audit and research. Some members of Cleft Teams are also involved in humanitarian work in developing parts of the world.



Figure 13 Cleft Team members

Following the recommendations of the CSAG report (Bearn *et al.*, 2001) the number of teams treating patients with OFC has been reorganised and centralised to 11 units across the UK and Ireland (Figure 14).

Name of Multidisciplinary Cleft Team	Location
Cleft Net East	Addenbrookes Hospital, Cambridge
North Thames Cleft Service	Great Ormond Street Hospital for Children St Andrew's Centre, Broomfield Hospital, Chelmsford
Northern and Yorkshire Cleft Service	Leeds General Infirmary Royal Victoria Infirmary Newcastle-upon-Tyne
Northern Ireland Cleft Service	Royal Victoria Hospital, Belfast
Northwest England, Isle of Man, North Wales Cleft Service	Alder Hey Hospital, Liverpool Royal Manchester Children's Hospital
Republic of Ireland	Children's University Hospital, Dublin Lady's Children's Hospital Crumlin, Dublin
Cleft Service in Scotland (CLEFTSIS)	Royal Hospital for Sick Children, Edinburgh Royal Hospital for Sick Children, Glasgow
South Wales South West Managed Clinical Network	Frenchay Hospital, Bristol Morriston Hospital, Swansea
Spires Cleft Service	Salisbury District Hospital The John Radcliffe, Oxford
Trent Cleft Service	Nottingham City Hospital
West Midlands Cleft Service	Birmingham Children's Hospital

Figure 14 Cleft Teams in the UK and Ireland. Adapted from McIntyre (2014a)

2.6.1 Care Following Diagnosis

Cleft care begins at birth or earlier if a diagnosis has been made at a prenatal ultrasound scan. A prenatal diagnostic rate of 28% of CLP and 2% of CP in Glasgow was found in a recent retrospective study of OFC births from 1999-2008. The findings were similar to other rates in the UK. Early diagnosis is likely to increase with the implementation of routine anomaly scanning (Paterson *et al.*, 2010).

If a prenatal diagnosis is made The Cleft Lip and Palate Association guidelines state the states "It is essential that telephone contact should be made with the (Cleft) Team before the parents leave the scanning department' (CLAPA 2001). If no complications are

anticipated with the birth the mother will attend her local maternity unit (Chalmers *et al.*, 2012).

In Scotland, following the birth of a baby with OFC, a standard has been set that 80% of babies and their parents will be visited by the designated National Managed Clinical Network for Cleft Service in Scotland (CLEFTSiS)(Figure 15) Network First Contact within 24 hours following diagnosis. The first member of the team to meet the new baby is most commonly the Cleft Nurse Specialist who will give support to the mother including feeding advice. Follow up should consist of a multidisciplinary team review within the first 2 months.



Figure 15 CLEFTSiS logo.

2.6.2 Surgery

A child with OFC may face multiple surgeries in their lifetime (Figure 16). If the cleft lip is wide, lip strapping may be appropriate prior to primary surgery.

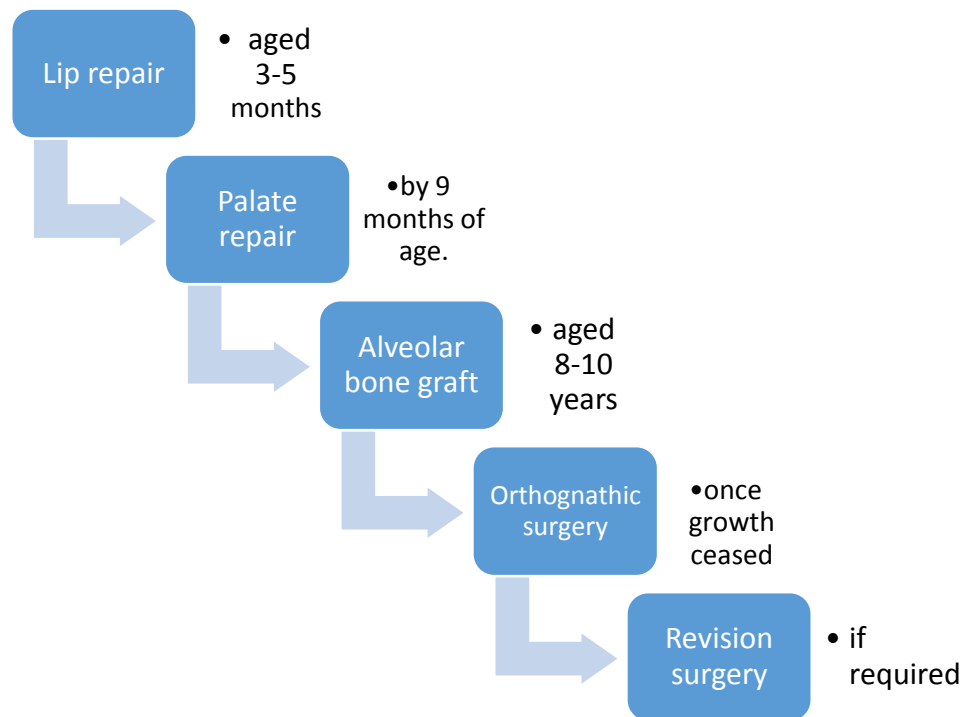


Figure 16 CLP surgeries and timings

Primary surgery includes closure of the lip which is routinely carried out between the ages of 3-5 months and closure of the palate before 9 months of age. Some centres, commonly in France, delay hard palate closure until later (6-60 months) to prevent disturbance to the growth centres and often requires the provision of a cover plate (Goodacre and Swan 2008). The debate about the optimum timing for lip and palate repair in relation to speech, psychological well-being and facial growth remains to be concluded. Several longitudinal research projects are being undertaken globally to answer this question.

Unless there is only mild notching of the alveolus, the secondary surgical step in the cleft care pathway is an alveolar bone graft. Any supernumerary teeth should be removed 3 month prior to bone grafting and may require a further general anaesthetic. This surgery is often thought of as the final 'compulsory' surgery (McIntyre 2014b). Cancellous bone is harvested routinely from the iliac crest and packed into the alveolar deformity and floor of

the nose. The bone graft facilitates the eruption of the maxillary canine, supports the alar base and supports the cleft segments. The success rate of this type of surgery has improved since the findings of the CSAG report (58% success rate) (Williams, *et al.*, 201) to 85% (Revington *et al.*, 2010). Any residual fistulae are often repaired during the same operation.

During adolescent growth the patients underlying skeletal pattern will become apparent.

The primary closure of the palate carried out at conventional times may severely restrict the growth of the maxilla in the anterior posterior direction (Mars and Houston 1990). Maxillary retrusion usually presents with an occlusal and skeletal III relationship. An assessment on a joint Orthognathic clinic is recommended at an early stage to advise the patient and their family of what is likely to be involved from both a orthodontic and surgical perspective (McIntyre 2014c). Timing of orthognathic surgery should be once growth has ceased.

Distraction osteogenesis may be considered in cases with severe maxillary retrusion (Figuerola *et al.*, 2004).

Revision surgery can be considered if a patient is not happy with the appearance of their lip.

Dermal fillers can be used if there is a lack of fullness of the tissues. A rhinoplasty is not contemplated until after orthognathic surgery as the surgical movement of the maxilla can affect the nasal profile.

2.6.3 Ear Nose and Throat and Audiology

One of the first investigations a new baby with cleft will undergo is a hearing screening. This is performed within the first four weeks postpartum. Hearing is reassessed at 6-9 months then repeated annually until the age of 5. Tests include otoscopy, audiometry and tympanometry.

As previously discussed in section 2.4.2 Hearing otitis media ('glue ear') occurs commonly in children with OFC. An additional surgery may be required to insert a small ventilation tubes ('grommets') to prevent fluid building up within the Eustachian tubes.

If a hearing impairment is diagnosed a hearing aid may need to be prescribed.

Audiology audit records are collected as per Table 2 and Table 3.

2.6.4 Speech and Language

Audiology, speech and language are all closely linked in cleft care. One of the most important goals is normal speech (Sell *et al.*, 2001).

Babies' first speech is described as 'babbling' which normally begins at around 6 months of age. Speech audit records are first collected following palate repair surgery. Where any speech difficulties present the speech and language therapists will work closely with the patient. As mentioned in section 2.4.3 Speech), velopharyngeal insufficiency can occur in OFC. To investigate this videofluoroscopy and or nasendoscopy examination can be used to visualise the problem area. Surgical intervention may be required to correct any structural anomalies (McIntyre 2014b).

Problems with articulation can be assisted by a technique called electropalatography (EPG). An intraoral custom-made EPG appliance is constructed with sensors on the palate area which are connected to a computer programme. When the tongue touches the sensors on the pronunciation of t, d and s sounds, the computer screen lights up providing a visual aid to assist with speech therapy. A randomised controlled trial found the EPG technique useful in the treatment of defective 's' sounds (Michi *et al.*, 1993). A recent Cochrane review

highlighted the limitations of the trial by Michi *et al.*, and highlights need for further (high quality) randomised controlled trials to be undertaken in this area (Lee *et al.*, 2009).

2.6.5 Psychology

Psychological support is on hand to both the child affected by OFC and the parents.

Whether the birth of a baby with OFC is anticipated or not the parents may need some support to come to terms with their child's diagnosis. As discussed in section 2.4.4

Psychology) teasing is commonplace and a child's self-confidence can be lowered.

Psychological input can be sought around the time of orthognathic surgery and into adulthood if required.

2.6.6 Dental Care

The developing dentition should be monitored by the patient's General Dental Practitioner as well as the specialist Paediatric Dental team, where available. Reinforcement of oral hygiene and dietary advice along with fluoride application and fissure sealants is essential to minimise dental disease that may complicate future orthodontic treatment and surgery (McIntyre 2014b). Specialist restorative treatment is sought if dental implants are required to replace missing teeth.

2.6.7 Orthodontics

The developing dentition will also be under review by the Orthodontic team. Orthodontic treatment often commences prior to alveolar bone grafting to expand the maxilla. A quad-helix appliance (or tri-helix if inter-alveolar width is severely restricted) is routinely fitted.

Patients with OFC commonly present with dental anomalies including hypodontia, transposition, structural anomalies supernumerary and impacted teeth (Menezes and Vieira 2008). Due to the complex nature of the dentition in cleft lip and palate any orthodontic

treatment using fixed appliances should be undertaken by an orthodontist who is part of a cleft team. Orthodontic alignment of the maxillary teeth may be carried out while the patient is still growing. If orthognathic surgery is required the patient will require pre-surgical orthodontics to decompensate the dental arches. The Orthodontist will also be involved in the production and management of speech prostheses such as electropalatography (EPG), palatal lift appliances and obturators for oronasal fistulae and clefts that have not been repaired due to medical reasons.

The Orthodontic team are also involved in audit of cleft care and routinely undertake data collection including photographs, radiographs, clinical data recording and impressions for study models.

2.6.8 Audit

Clinical audit is an essential tool in cleft care and records are collected to generate evidence base for best treatment protocols. This has been carried out on a national (Sandy *et al.*, 1998) and international level (Shaw *et al.*, 2001). Audit records include study models, photographs, radiographs, speech/audiometry/tympanometry records and patient/parent feedback. Timing for minimum records has been outlined by the World Health Organisation ((Organisation 2000). The timings for record collection for UCLP and BCLP are outlined in Figure 17. Local CLEFTSiS audit protocols are shown in Table 2 and Table 3.

WHO and CLEFTSiS recommends study models to be taken pre-surgery and at 5, 10 and 18-20 years of age for subjects with UCLP and BCLP.

Timing	Models	Lateral skull radiograph	Photographs	Speech/ tympanometry	Audiometry	Patient/parent satisfaction
Primary surgery	✓		✓			
3 years				✓*	✓*	
5/6 years	✓		✓	✓	✓	
10 years	✓	✓	✓	✓	✓	
18+ years	✓	✓	✓	✓		✓

* = If hard palate is closed.

Figure 17 Timing of minimum records for UCLP and BCLP. Adapted from WHO (2000).

Unilateral and Bilateral Cleft Lip and Palate:

0 - 5 years

Age	Models	Cephalogram	IO radiograph	Photographs	Speech	Audiology	Dental Health	Audit
Birth				✓				
4 – 8 weeks						✓		<ul style="list-style-type: none"> New born Hearing Screening followed by diagnostic assessment if indicated.
Pre-lip repair	✓			✓				
Post-lip repair				✓				
Pre-palate repair	✓			✓				
Post-palate repair					✓			
1 year						✓	✓	<ul style="list-style-type: none"> Audiogram, Tympanometry, & Otoscopy Dental Health (dmft)
2 years					✓	✓		<ul style="list-style-type: none"> Baseline speech assessment Audiogram, Tympanometry, & Otoscopy
3 years						✓	✓	<ul style="list-style-type: none"> Audiogram, Tympanometry, & Otoscopy Dental Health (dmft)
5 years	✓			✓	✓	✓	✓	<ul style="list-style-type: none"> CAPS-A Audiogram, Tympanometry, & Otoscopy Study models and/or photos- dental arch relationship (5yr index/HB) Orthodontic Audit Form Facial appearance Dental Health (dmft)

Table 2 CLEFTSiS audit records age 0-5 years for UCLP and BCLP.

Unilateral and Bilateral Cleft Lip and Palate:

6 - 20 years

Age	Models	Cephalogram	IO radiograph	Photographs	Speech	Audiology	Dental Health	Audit
Pre bone graft	✓		✓					<ul style="list-style-type: none"> Intraoral radiograph - outcome assessment of bone grafting
Post bone graft			✓					<ul style="list-style-type: none"> Intraoral radiograph - outcome assessment of bone grafting (Kindelan)
10 years		✓ & OPG		✓	✓	✓	✓	<ul style="list-style-type: none"> CAPS-A Study models - dental arch relationship pre- BG (GOSLON/HB) Orthodontic Audit Form Audiogram, Tympanometry, & Otoscopy Facial appearance/growth Dental Health (DMFT)
15 years			✓	✓	✓	✓	✓	<ul style="list-style-type: none"> CAPS-A Intraoral radiograph - outcome assessment of bone grafting on canine eruption (Bergland) Audiogram, Tympanometry, & Otoscopy Dental Health (DMFT)
20 years	✓	✓		✓				<ul style="list-style-type: none"> Facial appearance/growth

Table 3 CLEFTSiS audit records age 6-20 years for UCLP and BCLP.

Until 2012, both the Scottish audit records and the resultant audit data were uploaded onto the CLEFTSiS Excelicare database. Since 2012, only the key outcomes have been entered on to the National Clinical Audit System (NCAS) with the storage of the primary audit records being the responsibility of the individual NHS Board areas. The majority of records have specific measurements taken or indices recorded. The indices used to score surgical outcome will be discussed in depth in section 2.9 (Primary Surgery Outcome Indices in Cleft Lip and Palate).

The 'Care Pathway' (Figure 18) for UCLP highlights the interlinking of cleft care provisions, multidisciplinary team working, key clinical interventions and stages.

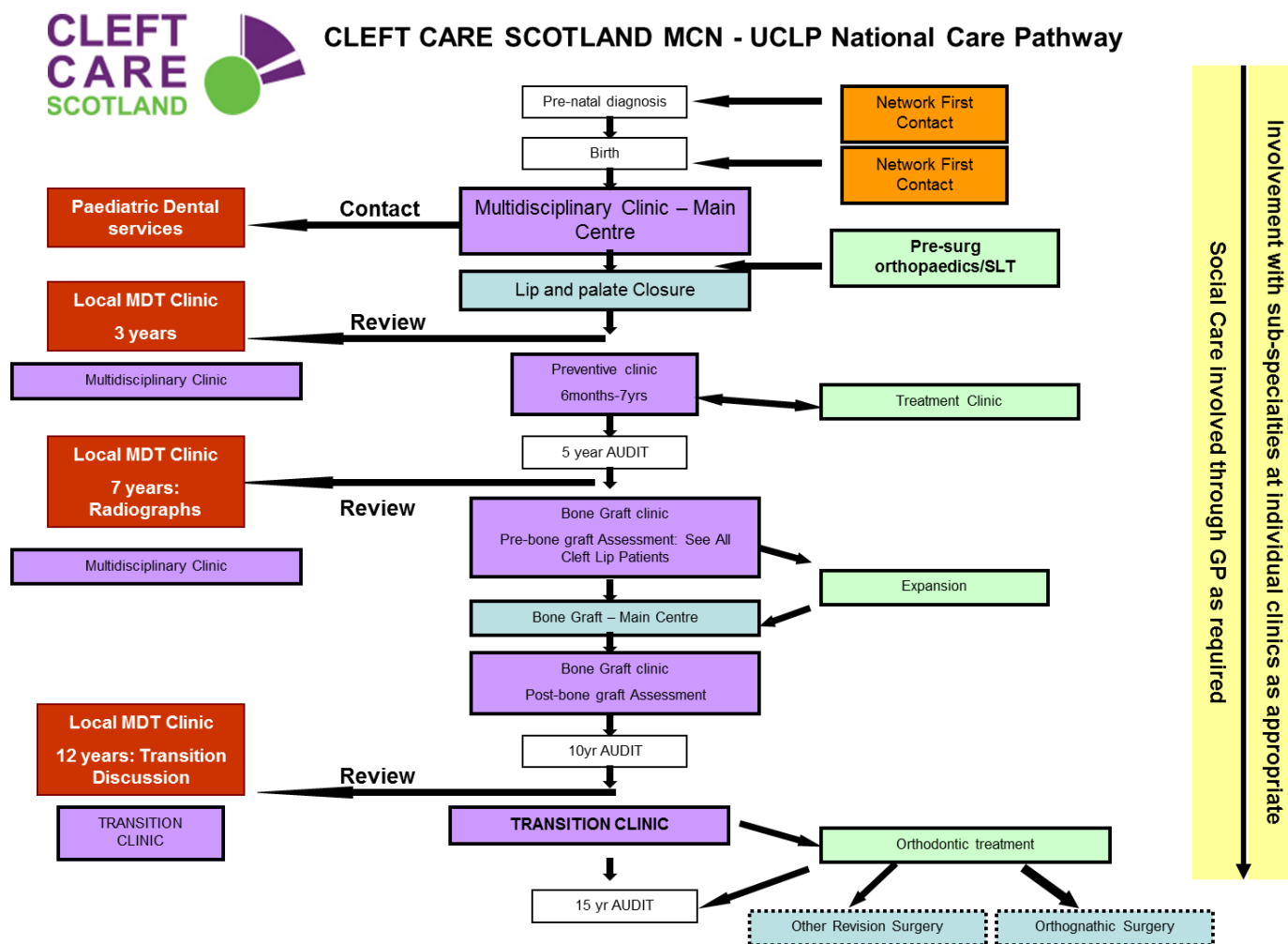


Figure 18 Cleft Care Scotland UCLP Pathway (note the re-branding of CLEFTSiS as Cleft Care Scotland).

2.7 Primary Surgery Outcome Indices in Cleft Lip and Palate

The World Health Organisation requires that dental indices meet the following requirements (Summers 1971):

- Reliable
- Valid
- Valid over time

Many indices have been developed to assess primary surgical outcome in patients with UCLP by scoring dental study casts.

The following indices are discussed GOSLON (Mars *et al.*, 1987), 5-Year-Old's Index (Atack *et al.*, 1997a), Huddart Bodenham (Huddart and Bodenham 1972), modified Huddart Bodenham (Mossey *et al.*, 2003) and EUROCARN Yardstick.

2.7.1 GOSLON

The GOSLON (**G**reat **O**rmond **S**treet, **L**ondon and **O**slo) Yardstick was developed by (Mars *et al.*, 1987) as a 'clinical tool' allowing the occlusions of children with unilateral cleft lip and palate to be placed into one of five categories reflecting their malocclusion and the potential complexity of orthodontic correction. The tool was created to assess those in the early permanent or late mixed dentition when malocclusions often become apparent. It is currently the most commonly used occlusal index in cleft care (Altalibi *et al.*, 2013).

Clinical Dimension	Unfavourable Features	Favourable Features
Anterior Posterior	<ul style="list-style-type: none"> • Severe class III • Reverse overjet with pre-existing dentoalveolar compensation 	<ul style="list-style-type: none"> • Class 2 div1
Vertical	<ul style="list-style-type: none"> • Reduced or open overbite 	<ul style="list-style-type: none"> • Deep overbite
Transverse	<ul style="list-style-type: none"> • Canine crossbites in smaller segment worse than molars crossbites 	<ul style="list-style-type: none"> • Absence of crossbite

Table 4 Features assessed in the GOSLON Yardstick.

A collective view of features thought to be of most significance to treatment outcome in UCLP patients in this age group were highlighted by the authors (Table 4). The anteroposterior clinical dimension was deemed to 'be of greatest clinical importance'. It was later found that overjet was the most significant component in predicting GOSLON scores (Morris *et al.*, 1994).

To test the features identified, 30 study models of untreated UCLP patients from The Hospital for Sick Children at Great Ormond Street, London were ranked by four orthodontists. Once ranked the models were seen to fall into 5 groups. The groups were numbered from 1 to 5 with increasing complexity of treatment required to correct their malocclusion (Mars *et al.*, 1987).

Master models were selected as representatives of each of the five categories giving a physical reference for assessors to compare patient models to. Instructions in using the Yardstick are to first examine the anterior posterior dimensions followed by the vertical and transverse dimensions.

Clinicians using the GOSLON Yardstick are required to undertake calibration training to ensure standardisation to allow scoring between cleft centres to be comparable. It has been shown that accuracy in carrying out GOSLON scoring increases if assessors undergo training in the use of this clinical tool (Sinko *et al.*, 2008).

Once developed and tested Mars *et al.*, (1987) went on to compare groups of patients with UCLP. It was found that the reliability of carrying out GOSLON scoring was highly reliable and there was no significant bias. Several other studies have gone on to compare groups of patients GOSLON scores and have found similar levels of reliability (Hathorn *et al.*, 1996, Mars *et al.*, 1992, Sinko *et al.*, 2008).

Group 1: Positive overjet with average inclined or retroclined incisors with no crossbite or open bite. Long-term outcome: excellent.
Group 2: Positive overjet with average inclined or proclined incisors with unilateral crossbite or crossbite tendency with or without open bite tendency around the cleft site. Long-term outcome: good.
Group 3: Edge-to-edge bite with average inclined or proclined incisors or reverse overjet with retroclined incisors. Unilateral crossbite with or without open bite tendency around the cleft side. Long-term outcome: fair.
Group 4: Reverse overjet with average inclined or proclined incisors. Unilateral crossbite with or without bilateral crossbite tendency with or without open bite tendency around the cleft site. Long-term outcome: poor.
Group 5: Reverse overjet with proclined incisors, bilateral crossbite, and poor maxillary arch form and palatal vault anatomy. Long-term outcome: very poor.

Figure 19 GOSLON categories. Adapted from Mars *et al.*, (1987).

The age of patients that can be scored using the GOSLON Yardstick is limited to those in the late mixed dentition and early permanent dentition (9 to 11 years of age). The underlying iatrogenic maxillary constriction may be masked at this age following alveolar bone grafting and or orthodontic treatment giving a underestimated impression of the outcome of primary surgery. The GOSLON Yardstick can only be used in patients with UCLP requiring the creation of a separate indices for other cleft types and age groups.

The nature of the Yardstick scoring requires a considerable level of clinical judgement meaning that assessors must be experienced orthodontists, ideally in cleft care. This prevents the delegating of time consuming scoring to other members of the dental team. A

degree of subjectivity is evident as each assessor is using their own expertise and experience to allocate the models to a category of potential treatment complexity.

The necessity for calibration involves the assessor attending a course and obtaining a set of reference models to carry out future scoring. The inconvenience and expense of having physically attend a course could potentially be avoided by the creation of digital reference models and an internet based training module as suggested by (Sinko *et al.*, 2008).

The GOSLON Yardstick generates a ordered categorical classification system. The data generated from carrying out GOSLON scoring of a group of patients does not lend itself to parametric scoring and is less statistically powerful than data output that is continuous and numerical.

2.7.2 The Five-Year Old's Index

The ability to detect and assess the outcome of primary surgery to correct palatal deformity in UCLP at an earlier age would potentially allow cleft surgeons to alter their practice sooner if poor audit results were recorded. Five year old UCLP patients are unlikely to have undergone any orthodontic camouflage of their occlusion or secondary surgery allowing the outcome of primary surgery to be assessed.

A decade on from the development of the GOSLON Yardstick, the creation of a potential measure of treatment outcome in a younger age group of patients with UCLP was explored (Atack *et al.*, 1997a). The authors aimed to create a similar index to GOSLON for 5 year old patients as they felt it was 'not entirely appropriate' to apply the Yardstick to this cohort (Figure 20). In contrast an earlier study found the GOSLON Yardstick a 'useful measure of longitudinal assessment of dental arch relationships' (Noverraz *et al.*, 1993).

Atack *et al.*, (1997a) selected 2 cases from each of the 5 defined groups to create the new index. The grouping by clinical features to give a predicted treatment outcome was very similar to the GOSLON Yardstick.

<i>Group</i>	<i>General Features</i>	<i>Predicted Long-Term Outcome</i>
1	Positive overjet with average inclined or retroclined incisors No crossbites/openbites Good maxillary arch shape and palatal vault anatomy	Excellent
2	Positive overjet with average inclined or proclined incisors Unilateral crossbite/crossbite tendency ± Open bite tendency around cleft site	Good
3	Edge-to-edge bite with average inclined or proclined incisors; or reverse overjet with retroclined incisors Unilateral crossbite ± Open bite tendency around cleft site	Fair
4	Reverse overjet with average inclined or proclined incisors Unilateral crossbite, ± bilateral crossbite tendency ± Open bite tendency around cleft site	Poor
5	Reverse overjet with proclined incisors Bilateral crossbite Poor maxillary arch form and palatal vault anatomy	Very Poor

Figure 20 General features of study models in the 5 Year Olds' Index. Adapted from Atack *et al.*, (1997b).

The 5 Year Olds' index has similar disadvantages as the GOSLON index in that it is limited to patients with UCLP, it is ordered categorical requiring rater clinical expertise and calibration to reduce systematic bias is recommended. In its favour the 5 year index has been shown to be reproducible and reliable (Atack *et al.*, 1997b).

2.7.3 Huddart Bodenham

Huddart and Bodenham (Huddart and Bodenham, 1972) created an alternative numerical classification for the evaluation of arch form in unilateral cleft lip and palate to supersede the categorical classifications that had been developed previously (Matthews *et al.*, 1970, Pruzansky and Aduss, 1964). The authors felt the earlier classifications were unsatisfactory as the categories they described were dissimilar, unordered and did not consider the full extent of the malocclusion. They also highlighted the non-numerical nature of the categories making statistical analysis difficult. On using the classifications from the previous literature, if a rater places a patient in a different category from another rater's score this implies that there is a 'fundamental type or nature of malocclusion' present in comparison to the system created by Huddart and Bodenham, where an inter-rater variation in score reflects a localised difference in local malocclusion.

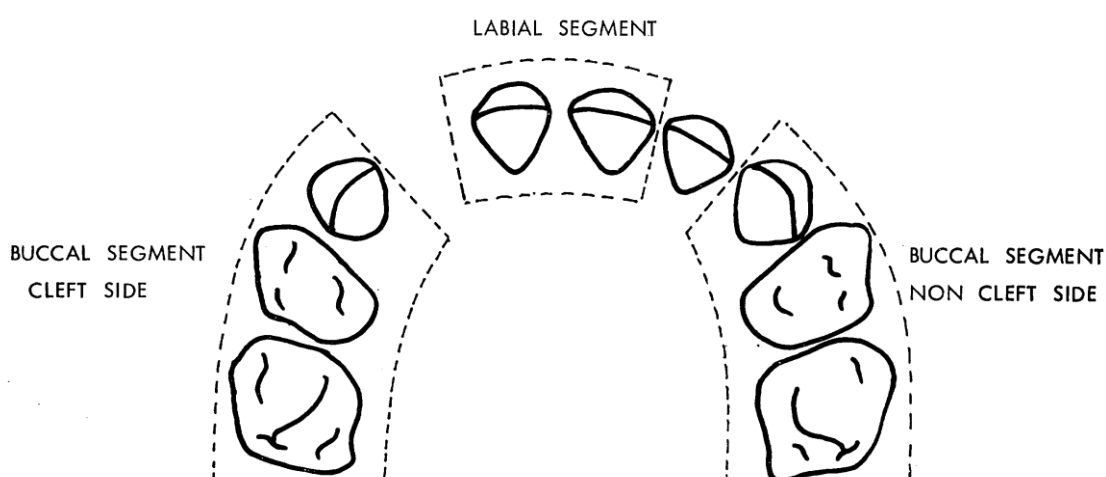


Figure 21 the division of the maxillary arch into 3 segments. Adapted from Huddart and Bodenham (1972).

The Huddart Bodenham scoring system was developed for patients with UCLP, aged 5 and in the deciduous dentition. The maxillary dentition is divided into 3 segments, 1 labial and 2 buccal (cleft and non-cleft) and their relationships with the mandibular arch are scored (Figure 21). Each tooth in the buccal segments is given a score from 0 to -2 and the central incisors from 1 to -2. An additive score over a continuous range of 2 to -18 is calculated for each patient. Lateral incisors were not included as they are frequently absent or malformed in patients with UCLP.

Although intended to use for patients with UCLP, Heidbuchel and Kuijpers-Jagtman (1997) successfully used the index to analyse transverse dental occlusion in subject with bilateral cleft lip and palate.

Observer consistency and reliability of each scoring system was analysed and were found to be equal and the observation of raters' abilities to undertake scoring was recommended.

2.7.4 Modified Huddart Bodenham

Mossey *et al.*, (2003) have since modified the technique for scoring maxillary arch constriction created by (Huddart and Bodenham, 1972). By extending the scoring of the dentition to the first permanent molars, after the age of 6 years, increased the versatility of the index allowing any age of patients to be given a modified Huddart Bodenham (MHB) score. If a canine is absent or yet to erupt, the midpoint of the maxillary alveolar ridge is used to score the relationship to the mandibular arch. Premolars are scored in the same way as deciduous molars and if absent the equivalent score to the neighbouring premolar is given or if both are not present the same technique for scoring a missing canine is used. In the scenario of a central incisor being absent the contralateral tooth is scored. For patients

aged from 3 to 6 years of age a total arch constriction score is given between –18 to +2 and for those over 6 years of age there is a maximum range of –22 to +2.

MHB is not restricted to UCLP and can be applied to any cleft subtype.

By carrying out MHB scoring of the reference models from the 5 Year and GOSLON Yardstick the authors validated the modified technique and its ability to discriminate between the categories set out in the indices. This was also replicated on a larger retrospective scale by Gray and Mossey (Gray and Mossey 2005). The nature of the MHB being a continuous scale increases its sensitivity and has the ability to detect the severity within the categories. The cumulative score from multiple individual categorical scores reduces the random operator error.

The non-subjective measurements in MHB scoring have the potential to be adapted into a computer programming algorithm and applied to digital study models. This would not be possible for GOSLON and 5 year scoring as this requires clinical expertise.

The lack of experience of treating cleft patients and the non-requirement for calibration would allow a wider range of staff including auxiliaries to carry out surgical outcome scoring using MHB. Scoring carried out by an orthodontic technician was shown to be reliable and highly correlated with cleft care practitioners (Gray and Mossey 2005).

MHB has the disadvantage that it does not take into consideration the underlying skeletal pattern which could be contributing to the presenting malocclusion and is likely to contribute to treatment complexity. The cumulative score does not differentiate between a localised crossbite that is severely reversed and a more generalised crossbite that presents 'edge to edge.' The ability to analyse the malocclusion in sections is a potential advantage

that is not possible with the single category surgical outcome scores. The vertical dimension of the occlusion is not incorporated. MHB scores the degree of crossbite rather than a favourable facial skeletal growth pattern.

A recent systematic review of indices in cleft lip and palate the authors state 'that the MHB Index be used to assess the malocclusions of all clefts of the lip and/ or palate of all ages' (Altalibi *et al.*, 2013).

2.7.5 The EUROCRAN Yardstick

A new outcome measure has been created by the EUROCRAN project that incorporates evaluating the surgical outcome of UCLP by scoring the dental arch relationship and the palatal morphology.

The EUROCRAN Yardstick is similar to the GOSLON AND 5-year-old index in that it has ordered categories but there are only 4 to score the dental arch relationship and 3 for the palatal morphology. The reduction in categories is due to the predominantly improving outcomes in cleft (Jones *et al.*, 2014) . Reference models are required to carry out EUROCRAN scoring.

Intra- and inter-rater reliability were found to be moderate - very good for the dental arch relationship scoring but less reliable for the palatal index (Fudalej *et al.*, 2011).

2.8 Occlusal Records

Occlusal records of the dentition are an essential tool in orthodontics and dentistry as they give a three dimensional representation of the occlusion. They can record the original occlusion, a progressive record of active treatment and a record of treatment outcome.

2.8.1 Plaster Study models

Study models are also routinely used in the fabrication of orthodontic appliances, diagnostic set ups, orthognathic surgery planning, surgical wafer construction and fixed or removable prosthesis. Study models are the current 'gold standard' and are cast from impressions of the dentition and poured in gypsum based dental plaster or stone. Impressions are defined as 'a negative likeness or copy in reverse of the surface of an object; an imprint of the teeth and adjacent structures for use in dentistry' (Glossary of Prosthetic Terms 2005). Study models are often utilised in research and audit and are still used in the conduct of professional exams in the UK Surgical Royal Colleges.

Drawbacks of conventional plaster models are that they are brittle, bulky, and heavy. Storage, transfer and retrieval are cumbersome (Joffe 2004, Keating *et al.*, 2008, McGuinness and Stephens, 1992).

Ideally, for medico-legal purposes study models should be retained indefinitely. To comply with the Consumer Protection Act 1987 records should be kept for at least eleven years for adults, and, for children for eleven years or up to age 25, whichever is the longer (BDA 2009).

'The current patient record is limited to a 2D representation of 3D anatomy, poor spatial accuracy, static in space and time, distortions and information voids' (Mah and Bumann

2001). Digital technology has revolutionised the storage and handling of orthodontic records (Sandler 2001). Digital clinical notes, photographs and radiographs are in regular use and the introduction of 'virtual study models' may allow the use of a fully electronic patient record for the orthodontic patient (Joffe 2004).

Technology developed in the 1990's and subsequent software refinements have allowed digital study models to be made available commercially (Fleming *et al.*, 2011). The models are created by scanning the 'hard copy' models to create in-direct digital study models. Since then, technology has been developed to intra-orally scan the dental arches, creating direct digital study models, eliminating the requirement for impression taking and casting of traditional plaster study models (Christensen 2008). In a survey of Orthodontists in the United States of America the use of digital models was 18%, which was a threefold increase from an identical survey 6 years previously (Keim *et al.*, 2008).

Digital models aim to eliminate the problems associated with plaster models as they have ease of access, storage (Keating *et al.*, 2008) and provide new benefits such as digital archiving and use in clinical and research studies (Ayoub *et al.*, 1997).

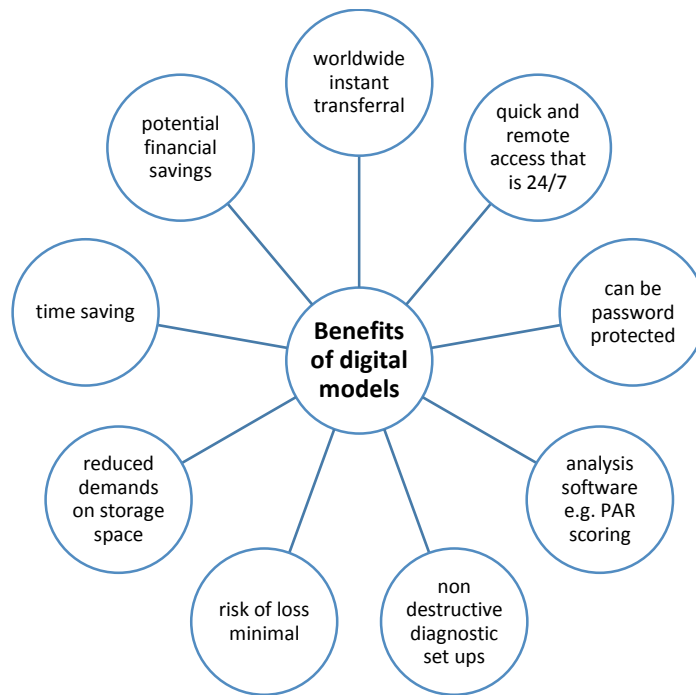


Figure 22 Potential advantages of digital study models.

2.9 Imaging of study models

Previous attempts have been made to archive study models to reduce demands on storage space by imaging them with photocopiers, photographs and holograms. Each are described in turn.

2.9.1 Photocopies

Images of study models have previously been captured by photocopying the occlusal surfaces to allow comparison of arch-forms and for taking intra-arch measurements. This method does not accurately represent three dimensional study models in two dimensions due to the convex surfaces of the models creating a positive error in measurements (Champagne 1992). Potential distortion of the photocopy image or shadowing could result in an error in landmark recognition. Al-Dashti *et al.*, (2005) found tooth dimensions measurements to be larger from photocopies in comparison to those taken directly from

study models. Archiving a photocopy of the maxillary and mandibular models within a patients' case notes could prove useful for monitoring pre and post treatment arch-forms but are not accurate enough for recording arch length or carrying out space analysis.

2.9.2 Photographs

An early version of two dimensionally digitising study models was created by QuickCeph in the mid 1990's (QuickCeph Systems, San Diego, USA) which involved photographing cast plaster models in the 5 standard views (front, right and left lateral, and upper and lower occlusal). The photographs were uploaded and stored within the QuickCeph software and allowed them to be viewed and the tooth widths could be measured to perform a space analysis. Saving digital images of models electronically reduces demands on storing the models, there is easier retrievability, transmission becomes more feasible (Ali, *et al* 2006) and is cost effective (Malik *et al.*, 2009) but there is limited ability to manipulate the models and the process of impression taking and plaster model construction is still required (Joffe 2004, Mah 2007). It has been shown for the purposes of medico-legal reporting that the same information can be obtained from photographs of study models and from plaster study models (Malik, *et al.*, 2009). Digital photography is readily available in the majority of orthodontic practices and is readily accepted by practitioners (Naidu and Freer 2013a).

2.9.3 Holography

Holograms of study models were created in an attempt to eliminate some of the problems of storing plaster study models (Schwaninger *et al.*, 1977). The reconstructed 3D image of the study models appears on a 2D film that could be filed within a patient's case notes. 'A laser is needed which produces a coherent (all light waves in phase), monochromatic (one single wavelength) light beam' (Schwaninger *et al.*, 1977). A high resolution photographic

plate records the interference caused by the phase difference between the beams. The original equipment was cumbersome and required demanding laboratory conditions and toxic developing chemicals. Technology developed in the 1980s allowed the creation of holograms more amenable to the clinical situation and required a holocamera, automatic developer, illumination and measuring elements. Impression taking and model casting was still required. Once cast, the models were scanned in standard dark room facilities using a holographic laser and were viewed on a special light box containing a halogen lamp. Once processed, the final hologram presents as a small plate that can be stored in the patients case notes (Romeo *et al.*, 1995). The subsequent image is three dimensional but static and once developed cannot be manipulated or utilised for appliance construction. The hologram is resistant to the majority of destructive agents apart from fire. They must be kept moisture free to retain image consistency (McGuinness and Stephens 1993). A prospective pilot study found that the use of holograms had consistent and increased availability in comparison to study models (Harradine *et al.*, 1990). Peer Assessment Rating (PAR) index scoring using holograms was found to result in significantly lower scores and greater random errors (McGuinness and Stephens 1993). The upper anterior teeth on a hologram obscure the lower labial teeth by casting a shadow (Ayoub *et al.*, 1997). Precision of depth measurements was poor and was found to be significantly increased in comparison to results from plaster study models (Keating *et al.*, 1984, Romeo *et al.*, 1995), this is thought to be due to the differing wavelengths between the hologram and the laser source. Holograms were regarded as a step towards creating a more easily achievable 3D record of the occlusion but the limitations of the technique outweighs the benefits, and thus they have failed to find a use in contemporary orthodontics.

2.10 Digitisation of Study Models

Advancing technology has allowed study models to be imaged in 3D and digitised via stereophotogrammetry, cone beam computerised tomography (CBCT) and laser scanning. More recently the ability to capture the occlusion directly via intra-oral scanning has been made available. Each are described in turn.

2.10.1 Stereophotogrammetry

Stereophotogrammetry is the technique of using 2 or more cameras to capture an object and has been used successfully in facial imaging (Hajeer *et al.*, 2004). Ayoub, *et al.*, (1997) described a new technique for archiving study models in 3D using a 'biostereometric technique'. A stereo-pair of video cameras were connected to a computer installed with a software algorithm to convert the video images into digital points which can be reconstructed into a polygon mesh. Distances, volumes, angles and areas can be measured on the reconstructed stereophotographic model. Bell and Siebert (2003), evaluated the accuracy of the technique and found no significant differences between measurements on plaster and stereophotogrammetry computer generated 3D images of the same study models. The precision of the 3D images was 0.27mm which was not deemed to be clinically significant. The digital files can be stored and viewed on a computer and sent to a 3D printer for fabrication of a plastic model. This technique does still require impression taking and casting of plaster study models and the purchasing and storing of the stereophotogrammetry equipment.

2.10.2 Cone Beam Computerised Tomography

CBCT is similar to conventional CT scanning in that the ionising x-ray source and sensors rotate around the patient or object. A lower dose of radiation is received by the patient as the source is divergent, forming a cone.

CBCT can be used to radiographically image the dental and craniofacial structures in 3D and is utilised in orthodontics, oral and maxillofacial surgery, implantology and restorative dentistry.

CBCT technology has been used to create 3D images of the dentition via scanning dental impressions, study models and the patient directly.

Wiranto *et al.*, (2013) compared measurements taken from study models, direct intra oral scans and CBCT scans of impressions. A difference of -0.04 to 0.16 mm was found with the CBCT scanned impression tooth width measurements in comparison to the study models. Significant differences were found but none exceeded 0.2mm, Bolton ratios from the CBCT models were also found to be significantly smaller. Although statistically significant differences were recorded the authors deemed them not to be clinically significant.

Explanations for under measuring were thought to be due to moisture loss resulting in shrinkage or the impression material, as they had to be posted to the scanning company.

CBCT scanning of impressions has the benefit of removing the need to pour and cast study models but the need for impression taking remains and there is an inevitable cost and risk of loss of dimensional stability in posting the impressions.

It is also possible to CBCT scan study models that have been cast from impressions but limited studies have used this technique and only the abstracts were available in English (Lv

et al., 2012, Wu *et al.*, 2010). Both studies found measurements taken from CBCT scans of plaster models were reduced but not to a clinically significant level and both advocate the use of this technique for digitising study models.

Creating 3D study models by directly CBCT scanning the patients' dentition is possible and eliminates the impression taking process. A study by Kau *et al.*, (2010) compared measurements of overbite, overjet and Little's Index of Irregularity using CBCT study models and digital models created by scanning impressions using the OrthoCad system (Cadent, Fairview, New Jersey). No statistical significance was found between the 2 methods of creating 3D digital study models.

A similar study was undertaken by Tarazona *et al.*, (2011) but they found some statistically significant differences between some of the tooth width measurements they made on models created by CBCT and from digitisation of plaster models, but again there were not thought to be clinically significant.

In contrast, validity of measurements made as part of a comprehensive study model analysis were found to be poor to moderate for some parameters by Luu *et al.*, (2014). They also found the time taken to analyse the digital CBCT generated study models could be doubled but this increase in analysis time should be offset against the time and expense of pouring and casting models.

The benefits of CBCT acquired models include the ability to view additional clinical information such as bone levels, root positions, temporomandibular joints (Kau *et al.*, 2010) and the potential to collect all diagnostic records from one a single investigation with the advances in imaging technology. The disadvantage of exposing patients to ionising radiation

cannot be ignored, as not all orthodontic patients require CBCT and making a scan for the sole purpose of acquiring study models cannot be justified.

2.10.3 Laser Scanning

Surface laser scanning is commonplace within industry to create 3D digital images of objects in a non-invasive manner. A limitation of the technique is that the beam of the laser cannot reach undercuts; this is addressed by capturing the object from multiple angles with software merging the images. A high-resolution charge-coupled device camera detects the laser beam's profile as it 'sweeps' over the object (Figure 23) (Barry 2011). The width and depth of the object can be measured by triangulating the distance between the surface and the reflected beam. It should be noted that the laser has difficulty when scanning material that is red in colour or that is highly polished.

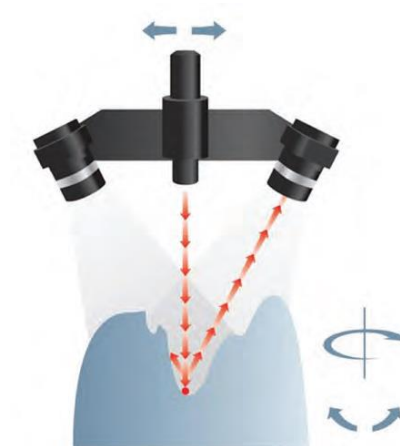


Figure 23 Laser and two cameras of R700 scanner used to view impression cavity [R700 Orthodontic Study Model Scanner[€] (3Shape, Copenhagen, Denmark)] Adapted from Barry (2011).

The scanning technology has been downsized and became available commercially for dentistry in 1999 (Fleming *et al.*, 2011) as 'in-office' study model and/or impression desktop

scanners. Once the image of the study model has been captured it can be saved and exported to viewing software. Common 3D file formats are Virtual Reality Modelling Language (.wrl) and stereolithographic (.stl) (Hajeer *et al.*, 2004) with .stl being the industry standard for digital design and can be used universally across software packages.

Both plaster study models and impressions can undergo scanning to create digital study models. The added benefit of scanning impressions is that it negates the requirement to pour the study models. The production of indirect study models requires the impression or cast model to be posted to proprietary services unless an 'in-house' scanner is available. This process introduces a delay in pouring the impressions introducing the risk of dimensional instability of the impression material (Torassian *et al.*, 2010) and there is a risk of models breaking or becoming 'lost in the post'. The procedure requires the upper model or impression and lower model or impressions to be scanned separately. To record the occlusion the models are articulated and scanned. A scan of the bite registration material is required when digitising impressions. Other systems require 'destructive scanning' in which the plaster model sectioned and each slice is scanned individually.

Once the scan has been taken a software package can be used to create a base for the digital models that simulates bases of trimmed orthodontic study models. Computer packages are available that will allow the digital models to be viewed, measured, analysed and linked to the patients digital case record (Barry 2011). If a 'hard copy' model is required when the original has been destroyed or was never cast (i.e. scanning of impressions) a 3D printing system can produce a model.

The process of laser scanning to create digital study models has many benefits as discussed earlier but the requirement for dental impressions with or without casting of the models remains.

2.10.4 Light-Emitting Diode (LED) Scanning

The technology has been developed to scan objects with an LED. This creates a fringe pattern which modifies during the scanning in width and phase in contrast to the linear scanning of a laser. Multiple patterns are collected by the scanner and are converted into 3D coordinates.

The blue LED emits shorter light wavelengths allowing for greater precision of the output virtual model (Logozzo *et al.*, 2008). The surrounding light levels need to be controlled or this can affect the contrast of the light signals. White and blue light LED scanners are 'eye-safe' as the light frequency used is below the intensity level to cause ocular damage.

2.11 Validity and Reliability of Indirect Digital Models

Accuracy and reliability are essential for diagnostic tools in healthcare. Several studies have been undertaken to validate the use of digital study models against the 'gold standard' of plaster study models. A variety of measurement parameters and indices have been scored and compared using both study model formats. A recent systematic review aimed 'to evaluate the validity of the use of digital models to assess tooth size, arch length, irregularity index, arch width and crowding versus measurements generated on hand-held plaster models with digital callipers in patients with and without malocclusion' (Fleming *et al.*, 2011). The findings of the review and relevant literature are summarised in Table 5 and discussed in turn.

Authors	Method	Sample	Examiners	Measurements	Findings
(Tomassett <i>et al.</i> , 2001)	OrthoCad vs digital callipers measurements from plaster models.	n=22	1	Bolton ratio	No statistically significant differences existed between the methods used to measure tooth-size discrepancies with the Bolton analysis.
(Bell 2003)	C3D-builder (stereophotogrammetry) vs digital callipers measurements on plaster models	n=22	1	Transverse and sagittal linear measurements	Average difference between measurements of dental casts and 3D images was 0.27 mm and was not statistically significant ($P < 0.05$).
(Santoro <i>et al.</i> , 2003)	OrthoCad vs digital callipers measurements from plaster models	n=76	2	Tooth size, OJ & OB	Digital tooth width and OB statistically significantly smaller ($p < 0.05$, $p = 0.0124$). Magnitude of 0.16 mm to 0.49 mm deemed not clinically significant. No difference in OB.
(Quimby <i>et al.</i> , 2004)	OrthoCad vs digital callipers measurements from Dentoform and plaster models	n=50	10	Tooth size, arch length, transverse, dimensions, OJ, OB, space analysis	Small differences between plaster and digital model measurements but were statistically significant ($P < 0.0001$) apart from mandibular inter-canine width and mandibular space required. Not stated if clinically significant.
(Mayers <i>et al.</i> , 2005)	OrthoCad vs plaster models	n=48	1	PAR	No significant differences were found between overall PAR scores of plaster and digital models ($p = 0.82$)
(Stevens <i>et al.</i> , 2006)	Emodels vs digital callipers measurements from plaster models	n=24	3	Bolton ratio, PAR and	No difference of mean measurement was clinically significant for Bolton 6 and 12 (0.04 and 0.38 mm, respectively), any arch length

				constituent measurements	(range, 0.20-0.59 mm), PAR score (range, 0.04-0.83), overjet (0.01 mm), or overbite (0.30 mm).
(Mullen <i>et al.</i> , 2007)	Emodels vs digital callipers measurements from plaster models	n=30	1	Bolton ratio and time taken to calculate ratio.	No significant difference between the Bolton ratio calculated on plaster and digital models ($p=0.86$). Calculating Bolton ratio on digital models was significantly quicker ($p<0.00001$). On average it was 65 seconds slower using the plaster models to calculate the ratio.
(Goonewar dene <i>et al.</i> , 2008)	OrthoCad vs digital callipers measurements from plaster models	n=50	1	Tooth size–arch length discrepancies, arch lengths and irregularity	High correlations between plaster and digital models for tooth size–arch length discrepancies and irregularity index. Significant difference ($P<0.05$) on measuring lower arch length, not on upper.
(Keating <i>et al.</i> , 2008)	Easy3D Scan vs digital callipers from plaster models	n=30	1	Transverse and sagittal measurements of linear dimensions	Mean difference of measurements 0.14mm, not statistically significant ($P=0.237$). Statistically different measurements in the 'z' plane (clinical crown height of all the teeth) ($P<0.001$).
(Redlich <i>et al.</i> , 2008)	ConoProbe (holographic sensor) digital callipers measurements from plaster models	n=30	1	Tooth width, arch length and crowding	Linear measurements were found to be statistically smaller ($P<0.05$) but clinically acceptable (0.18–0.28 mm). Significantly less ($p=0.02$) crowding found in severely crowded models to a clinically important level of 1.19–3 mm.
(Leifert <i>et al.</i> , 2009)	OrthoCad vs digital callipers measurements from plaster models	n=50	2	Tooth width and arch length for space analysis.	No statistically significant difference in mandibular models. Small (0.4 mm) but statistically significant difference in the space analysis measurements on maxillary models but deemed not clinically significant.

(Veenema <i>et al.</i> , 2009)	Digimodel vs plaster models.	n=30	2	ICON	No statistically different values were found for the total ICON score on either plaster or digital models.
(Horton <i>et al.</i> , 2010)	Emodels (laser scanning) vs digital callipers measurements from plaster models	n=32	1	Tooth size	Digital measurements slightly overestimated plaster model measurements but small bias and strong correlation deemed not clinically significant.
(Sharma <i>et al.</i> , 2013)	Plaster models vs digital study models	n=30	4	IOTN	No difference between plaster and digital models in either component of IOTN. Less agreement from digital models on aesthetic component.

Table 5 Summary of indirect 3D scanning literature.

2.11.1 Transverse dimensions

A commonly performed measurement during orthodontic treatment is to measure and monitor arch width via recording the inter-canine, -premolar and -molar widths. Small differences were detected between the means of measurements taken on plaster and digital models, but were thought to be below a clinically significant level (Fleming *et al.*, 2011).

2.11.2 Tooth Size

Several studies looked at tooth size and height measurements which can then be included in a Bolton analysis. Differences of less than 0.3mm were found and again seen to be not clinically significant. Incorporating tooth widths into a Bolton analysis was also seen to be acceptable using digital models (Mullen *et al.*, 2007, Stevens *et al.*, 2006, Tomassetti *et al.*, 2001).

2.11.3 Irregularity Index

Differing results were found in the 2 studies that looked at measuring Little's Irregularity Index (Little 1975). Goonewardene *et al.*, (2008) found correlation to be high between plaster and digital models but Stevens *et al.*, (2006) found a significant underestimated difference of 3.7mm.

2.11.4 Inter-arch occlusal features

It is important to be able to accurately measure inter-arch occlusal features as well individual intra-arch findings. Overjet and overbite has been shown to have high agreement between digital and plaster models by several authors (Quimby *et al.*, 2004, Santoro *et al.*,

2003, Stevens *et al.*, 2006). As well as excellent overjet agreement Stevens *et al.*, (2006) found a high correlation in centreline agreement between digital and plaster models.

2.11.5 Occlusal Indices

Indices of treatment need and outcome are routinely measured from plaster study models and include the PAR(Richmond *et al.*, 1992), American Board of Orthodontics (ABO) (Casko *et al.*, 1998) scoring and the Index of Complexity Outcome and Need (ICON) (Daniels and Richmond 2000). The ability to accurately carry out scoring of indices using digital models would allow, if required, multiple sets of models to be sent electronically for research, referral, consultation and audit purposes. Index scoring incorporated many of the inter- and intra-arch features previously validated for digital measurements. As well as being accurate the measurement from digital models are required to be reliable both for inter- and intra-examiner scoring.

Veenema *et al.*, (2009) found mostly statistically insignificant differences when ICON scoring was carried out on plaster and digital study models. The authors concluded that 'computer-based models appear to be as accurate and reliable as ICON scores on plaster models.'

Two studies (Mayers *et al.*, 2005, Stevens *et al.*, 2006) included in the review found PAR scoring from digital models to be reliable and would offer a clinically acceptable replacement for plaster models. Mayers *et al.*, (2005) suggest that the reliability of PAR scoring from digital models would allow the creation of an online PAR calibration exercise.

Limitations in the software used to carry out ABO scoring has adversely affected the results of several studies. Moreover, difficulties in assessing the buccolingual inclination of the teeth have been noted (Costalos *et al.*, 2005, Okunami *et al.*, 2007). The software has since been upgraded to resolve this (Hildebrand *et al.*, 2008). Occlusal contacts (Hildebrand *et al.*,

2008, Okunami *et al.*, 2007) and overjet (Hildebrand *et al.*, 2008) were also shown to be statistically significantly different between plaster and digital models. These differences contribute to a significantly increase in overall ABO scores with digital models, which has a clinical effect and may alter whether an examination candidate passes or fails. The consensus is that plaster models for ABO cannot currently be replaced by digital models (Hildebrand *et al.*, 2008). However, it should be noted that the UK Surgical Royal Colleges all accept digital models for specialty membership examinations in Orthodontics.

Sharma *et al.*, (2013) found no difference between plaster and indirect digital study models for scoring IOTN. A lower level of agreement was found with the aesthetic component of the index, but this is thought to be due its larger 10 point scale and its subjectivity.

2.11.6 Time Taken

It has been suggested that the analysis of digital models is less time consuming than their plaster counterparts (Horton *et al.*, 2010, Mullen *et al.*, 2007, Tomassetti *et al.*, 2001). The potential for time saving is possible for not just the analysis process. Less laboratory technician time is needed when impressions are scanned to create digital models when compared to pouring plaster models. The time taken to retrieve models from storage will be removed and the ability to electronically send models worldwide will allow quicker acquirement of models. Removing the impression taking process by directly scanning the dentition to create digital models could potentially increase the chairside time but reduce the processing time.

The systematic review (Fleming *et al.*, 2011) concludes that 'Digital models offer a high degree of validity when compared to direct measurement on plaster models; differences between the approaches are likely to be clinically acceptable.'

2.12 Intra-oral scanning

The accuracy of impression taking and casting to create regular plaster study models is influenced by the material, tray and technique used. Each stage can introduce error reducing the overall accuracy (Yuzbasioglu *et al.*, 2014). Impressions can be uncomfortable for the patient and can heighten anxiety particularly for those who experience a sensitive gag reflex (Kravitz *et al.*, 2014). Eliminating the need for impressions and replacing them with direct digital scans of the dentition could potentially reduce the human and or material errors, improve accuracy and reduce the potential of sensitivities to the materials (Roberta *et al.*, 2003).

The concept of creating an 'optical impression' of the dentition was first described by Dr Francois Duret in 1973. His concept was based on computer-aided design/computer aided manufacturing (CAD/CAM) which was being used in industry and his aim was to apply this technology to dentistry.

The first intra-oral scanner was created in the early 1980's (Mörmann 2006) and was incorporated into the CEREC® by Sirona Dental Systems LLC (Charlotte, NC) system for restorative dentistry. Since then several manufacturers have developed intraoral scanners for restorative and orthodontics purposes.

Non-contact optical technologies are utilised to create an intra-oral map. These include such as confocal microscopy, optical coherence tomography, 3D in motion video, triangulation, interferometry (Figure 24) (Kravitz *et al.*, 2014). Data points are collected using a scanning unit or hand held wand, and fed back to a workstation and can be viewed on a monitor.

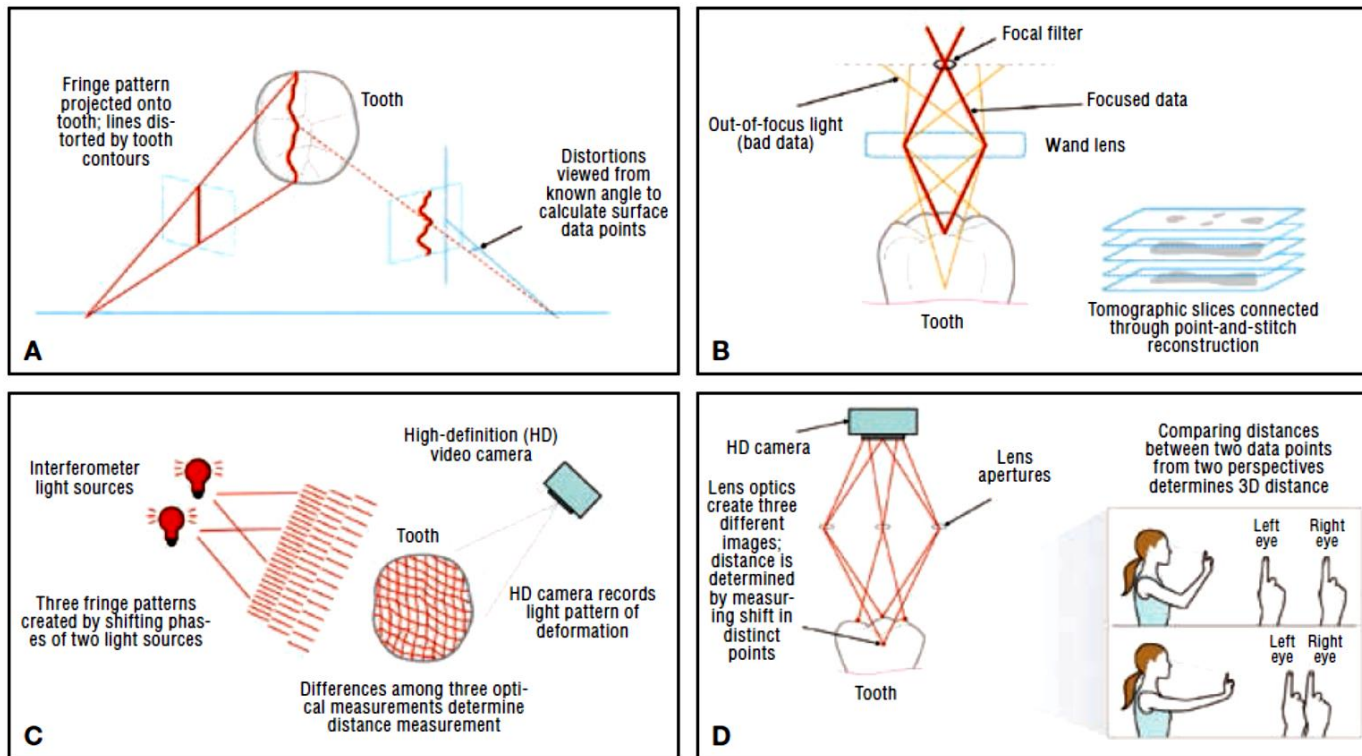


Figure 24 Common digital technologies. A. Triangulation. B. Parallel Confocal imaging. C. Interferometer light sources. D. Three dimensional in motion video imaging. Adapted from Kravitz *et al.*, (2014)

2.12.1 Triangulation

The triangulation technique utilises the Pythagoras theorem to calculate the distance from the laser source to the object as all the remaining angles and distances are known. A reflective titanium or zirconium-oxide powder is applied to the tissues prior to scanning to give an increase in surface data points and a uniformly reflective surface. Excellent moisture control is required to prevent the powder being washed away by saliva.

2.12.2 Confocal imaging

A beam of light is passed through a pinhole onto the target object and is reflected back via a mirror. The sensor only captures confocal (in-focus) light eliminating out of focus data

increasing the accuracy of the scan. The slices of data received are 'stitched' together to recreate the 3D surface digitally.

2.12.3 Interferometry

Accordion fringe interferometry (AFI) requires 2 light sources to create a 'fringe pattern' of light that is projected across the object. The light is distorted by the object and creates a 'fringe curvature'. The data is captured by a video camera positioned at a set point. Known geometry between the camera and laser source enable the AFI algorithms to digitize the surface of the object being imaged.

2.12.4 3D In-motion Video

A trinocular arrangement of 3 small high definition video camera captures the object from 3 aspects. A sensor located behind the cameras converts the light energy into electrical signals. By calculating the distances between 2 points from 2 perspectives the 3D data can be created. A powder coating is required for this 3D scanning technique but a lesser covering is required than in triangulation imaging (Kravitz *et al.*, 2014).

2.12.5 Validity and Reliability of Direct Digital Models

The objectives of Cuperus *et al.*, (2012) were to determine the validity and reproducibility of measurements taken from 10 dried human skulls, direct digital models and 3D printed stereolithographic models. The authors stated that to their knowledge no such study had been undertaken previously. The intraoral scanner used was the Lava Chairside Oral scanner (Lava, 3M ESPE, Seefeld, Germany). Two experienced observers repeated the measurements on 4 separate occasions.

Relatively small but statistically significant differences in measurements were found between 34% of those taken from the skulls and digital models. The measurements taken from the digital models were generally smaller than those from the skulls. If any data points were missed from the direct scan, from difficult areas to scan e.g. contact points, the software used had built in algorithms to correct for missing data. These small areas of automatically computer generated data may have affected the accuracy of the measurements. Smaller measurement errors were recorded on the digital models than those taken using digital callipers from the skulls and stereolithographic models, indicating a higher reproducibility for the digital measurements. A proposed explanation for this was the ability to zoom in on the models on a digital screen may result in smaller errors.

As this study was deemed to be the first to attempt to validate direct digital study models the authors were only able to compare their results with similar studies carried out using indirect digital models. The results from the direct scans, although found to be significantly different to those from the skulls, the differences were small and comparable with validation studies on digital models produced with an indirect method (Goonewardene *et al.*, 2008, Keating *et al.*, 2008, Santoro *et al.*, 2003, Stevens *et al.*, 2006, Tomassetti *et al.*, 2001). The conclusion was made that measurements on stereolithographic models and digital models made with an intraoral scanner are valid and reproducible (Cuperus *et al.*, 2012).

A previously mentioned validation study was carried out by (Wiranto *et al.*, 2013) who looked at linear measurements and Bolton analysis on 22 plaster models, direct intraoral scans and CBCT scans of alginate impressions. This study also used the Lava Chairside Oral scanner (Lava, 3M ESPE, Seefeld, Germany). This intraoral scanning system requires the

application of a thin layer of titanium oxide powder prior to scanning. No measurements made from the direct digital Lava models were statistically significantly different from those made using the 'gold standard' plaster models. The Bolton analyses performed on the direct digital models were smaller than those from the plaster models to a statically significant level. The difference did not exceed 1.5mm which was deemed clinically insignificant by Proffit (2013). The Intra-class correlation coefficients for the examiners were in excess of 0.90.

It was concluded that 'both intraoral scanning and CBCT scanning of alginate impressions are valid, reliable, and reproducible methods to obtain dental measurements for diagnostic purposes' (Wiranto *et al.*, 2013).

Naidu and Freer (2013b) also found a statistically significant difference between plaster and direct digital models, created with iOC intraoral scanner (Cadent, Carlstadt, NJ), when carrying out Bolton analyses. In contrast to the previous study a significant difference in tooth widths was also detected when measuring digital models. As in the findings of the previously discussed validation studies (Naidu and Freer, 2013a, Wiranto *et al.*, 2013) differences were deemed to be clinically insignificant. Again intra-class correlation coefficient values were high (all exceeding 87%) in this most recent study demonstrating excellent reliability and reproducibility (Naidu and Freer 2013b).

A recent study by (Grunheid *et al.*, 2014) superimposed direct and indirect 3D models of patients and found the biases to within a clinically acceptable range of 0.5mm. They also assessed the scan time and patient acceptability which is discussed in section 2.11.6 Time Taken.

Intra-oral scans have also been used to fabricate orthodontic retainers (Vasudavan *et al.*, 2010). The orthodontists in the study preferred the retainers made from the intra-oral scans.

A variety of intra-oral scanners have been approved to create digital models for orthodontic aligners (Jones 2008, Kravitz *et al.*, 2014) and for indirect bonding of orthodontic brackets (Garino and Garino, 2012).

Authors	Method	Sample	Examiners	Measurements	Findings
(Vasudavan <i>et al.</i> , 2010)	All patients had a conventional impression and an intra-oral scan to fabricate retainers.	n=24	2	Clinical acceptability of retainer fit. Orthodontists' retainer preference. Patient preference.	No difference in clinical acceptability of retainer fit between 2 techniques. Orthodontists significantly preferred retainers made via intra-oral scans. 77% of patients preferred the intra-oral scan.
(Cuperus <i>et al.</i> , 2012)	Stereolithographic models and digital models were made from scans of dry skulls.	n=10	2	Transverse distances, mesiodistal tooth widths, and arch segments.	Statistically significant differences were found between stereolithographic and digital models. These differences were considered to be clinically insignificant. Digital models had fewer statistically significant differences than the stereolithographic models.
(Wiranto <i>et al.</i> , 2013)	Intra-oral scans and CBCT scans of alginate impressions vs plaster models	n=22	3	Tooth width and Bolton analysis.	Tooth width measurement from the 2 digital techniques were not significantly different from the plaster models ($p>0.05$). Bolton ratios calculated from the digital models were significantly different ($p<0.05$), but were deemed to potentially not clinically significant (1.5mm)
(Naidu and Freer, 2013b)	Plaster casts vs direct digital models from intra-oral scans.	n=30	3	Tooth width and Bolton analysis.	Statistically significant differences were found between mean tooth widths ($p=0.0083$) and Bolton ratios ($p=0.0354$ and $P<0.0001$) with the 2 methods, the discrepancies were deemed to be clinically insignificant.

(Grunheid <i>et al.</i> , 2014)	Direct digital models from intra-oral scans vs indirect digital models from scans of alginate impressions. 5 sets of impressions were also cast in plaster. The scans were superimposed.	n=15		Accuracy, scan time, and patient acceptance.	Routine impression taking was significantly quicker ($p < 0.0001$). No difference was found when processing was included in the time taken ($p = 0.0649$). Biases for individual tooth size and arch length were found to be within clinically acceptable levels (< 0.5 mm). 73.3% of the patients preferred impressions because they were “easier” or “faster,” 26.7% preferred the scan because it was “more comfortable.”
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Table 6 Summary of literature regarding validity and reliability of direct digital models.

The evaluation of digital study models is a 'hot topic' in dental research. The literature currently published (Table 6) is generally positive with some minor differences between the current 'gold standard' of plaster models and digital mediums recorded and the majority being below a clinically significant threshold. Further well-designed clinical research investigating the use of digital models, and in particular direct scanning in orthodontics is required to increase the body of evidence before meaningful recommendations can be made. The ability to completely remove the impression taking in orthodontics and cleft care would require studies validating the use of intra-oral scans to create the full range of orthodontic appliances. The technique would also have to be shown to be applicable to all ages and sizes of patients including neonates.

2.13 Imaging of study models for analysing dental arch relationships in cleft lip and palate

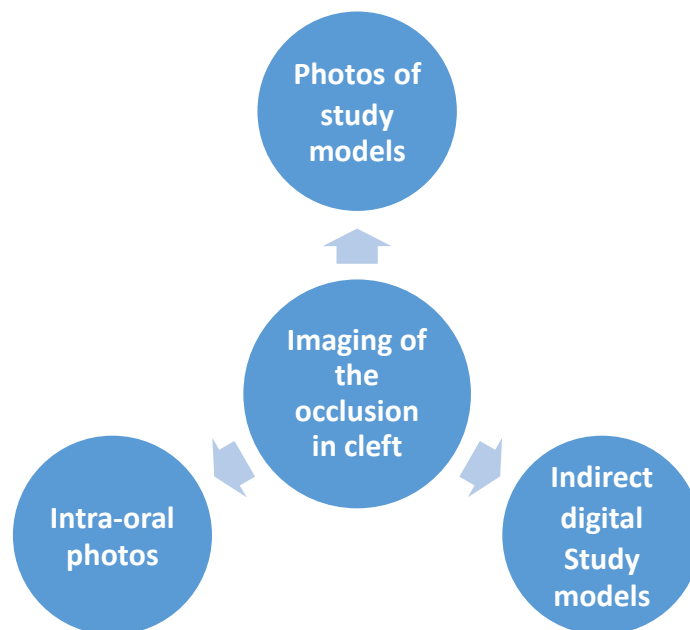


Figure 25 Imaging techniques.

The ability to record and image the occlusion in cleft lip and palate is essential for undertaking inter-centre research and audit. Uniting multiple researchers with clinical records is inconvenient, time consuming, financially demanding and risks the loss and/or damage of the records. Different methods of imaging the occlusion in cleft have been attempted to address these difficulties.

2.13.1 Photographs

A standardised technique of photographing plaster study models obtained from patients with cleft lip and palate has been performed by various authors. Digital photographs can be

sent easily via email or uploaded to a password protected website for researchers and clinicians to access. Online training and calibration modules could be created using a bank of images.

Nollet *et al.*, (2004) presented photographs of study models via a PowerPoint to examiners who then gave them a GOSLON score. Standard photographs were taken occlusally of each arch, from a frontal perspective and from the right and left sides, all with a plain black background. Photographs of the reference models were printed out and made available during GOSLON scoring. High intra- and inter-observer agreement for the GOSLON classification on dental casts and photographs was found. It was noted that the examiners found it difficult to assess the overjet in the 2D photographic images. An under or over judgement of the overjet may affect the GOSLON score given to a set of models, particularly in the lower categories. Similar difficulties were experienced on analysing dental arch relationships in BCLP from photographs (Leenarts *et al.*, 2012).

Ali *et al.*, (2006) successfully carried out MHB scoring on photographs of study models of 5 year old patients with UCLP. They concluded 'Digital photographs of dental casts of 5-year-olds with UCLP proved to be a reliable tool for assessment of dental arch relationships using the modified Huddart/Bodenham system.'

Directly photographing the occlusion has similar advantages to photographing study models but in addition removes the need to take dental impressions and may be slightly less traumatic for younger patients. Indices of cleft treatment outcome could theoretically be applied to intraoral photographs of the patient in occlusion. This was investigated by Liao *et al.*, (2009) using the GOSLON Yardstick and McAuliffe *et al.*, (2010) looked at the 5 Year Old Index. Both studies found clinical photographs a reliable alternative to study models.

Difficulty standardising clinical photographs was experienced by both authors and McAuliffe *et al.*, (2010) had difficulty obtaining complete records for the younger age group. The examiners found it difficult to identify crossbites (McAuliffe *et al.*, 2010) and overjet (Liao, 2009) from the photographs. The ability to manipulate and rotate images of the occlusion using 3D digital models would potentially eliminate some of the difficulties experienced when assessing treatment outcome from photographs.

2.13.2 Indirect 3D Scanning

A commercially available desk top model scanner [R250 Orthodontic Study Model Scanner (3Shape A/Copenhagen, Denmark)], was used by Asquith and McIntyre (Asquith and McIntyre 2012) to validate the use of digital models as an alternative to conventional plaster study models for scoring in patients with UCLP. Archived study models of 5 year old UCLP patients (n=30) underwent 3D scanning and were then scored using the 5 Year Old Index and MHB. The examiners were able to view and manipulate the digital models on a computer screen using the Ortho-Analyzer™ (3Shape A/S) software package. No statistically significant differences were found between the plaster and digital models. The authors noted that their study was limited to 5 year old patients and that carrying out a similar study looking at older patients and those with bilateral clefting would be beneficial.

A similar study was carried out by Chawla *et al.*, (2013) using the R640 3Shape Desktop study model scanner (3Shape A/S, Copenhagen, Denmark). A slightly larger cohort of 5 year old study models were analysed (n=45). The results showed the 3D digital models were reliable and reproducible for scoring for scoring treatment outcome with the 5 Year old Index.

Study models of bilateral cleft lip and palate patients aged 6, 9 and 12 underwent digitalisation and were viewed using the Digimodel programme (Orthoproof, Doorn, the Netherlands) in a previously mentioned study by Leenarts *et al.*, (2012). The original plaster models, photographs of the models and the 3D digital models were all scored using the BCLP Yardstick and no significant differences between the mediums were found.

The GOSLON Yardstick was applied to digital 3D models and plaster study models with a high degree of reproducibility and repeatability (Nicholls *et al.*, 2014, Nollet *et al.*, 2004). Computed tomography scanning with the 3MUnitek Lava™ (3MUnitek, North Ryde, Australia) converted the plaster models into 3D digital models.

GOSLON scoring was also carried out on plaster study models, 2D photographs and 3D indirect digital study models by (Dogan *et al.*, 2012, Servet *et al.*, 2012). Both 2D and 3D imaging had good reliability in comparison to the conventional plaster models. The 3D digital models and the plaster models showed better agreement results than other pairings but not to a significant level.

The current literature indicates that 3D digital study models of cleft patients are a valid alternative to the current 'gold standard' of plaster study models. This digitisation technique can be implemented for archiving pre-existing models. Prospective data collection using this technique will still require impression taking and casting of plaster models. For the purpose of research and audit having complete records is invaluable. Impression taking is thought to be less invasive than other records taken at cleft audit clinics but it is often upsetting for the child (Clark *et al.*, 2007).

Removing the requirement for impressions completely and replacing them with intraoral 3D scans would eliminate this sometimes distressing clinical procedure, potentially increasing

compliance with record collecting, could prove cost effective by reducing the cost of materials and free up orthodontic laboratory technician time. The technique of imaging the dentition via intra-oral scanning in cleft care has yet to be reported in the literature at the time of writing.

CHAPTER THREE: AIMS AND HYPOTHESES

3.1 Aims

1. To assess the reliability of intra-oral 3D scans as an alternative to study models for the assessment of surgical outcome of unilateral cleft lip and palate.
2. To determine patient and parent/carer acceptability of dental impressions and intra-oral 3D scans.

3.2 Hypotheses

1. There is no difference in the reliability of scoring surgical outcomes using the GOSLON and MHB indices on plaster and digital 3D study models.
2. There is no difference in patient and parent/ carer acceptability of routine dental impressions and intra-oral 3D scanning.

CHAPTER FOUR: MATERIALS AND METHODS

4.1 Study Design

This prospective study was designed to assess whether three dimensional digital models created by intra-oral scanning of 5-21 year old patients with cleft lip and palate can reliably be scored using the modified Huddart/Bodenham index and GOSLON Yardstick. Plaster study models, direct and indirect digital study models of the participants were scored by three examiners.

Ethical approval was required as the study involved clinical procedures on adult and child participants. The research protocol and accompanying patient information sheets (PIS), consent forms and questionnaires were reviewed and approved by West of Scotland Research Ethics Service.

As per the requirements of the Scottish Executive Health Department Research Governance Framework for Health and Community Care, the University of Dundee and NHS Tayside agreed to sponsor the study as co-sponsors.

Caldicott Guardian approval was obtained from NHS Greater Glasgow and Clyde as the study employed patient identifiable data.

A formal request for patient data was approved by the CLEFTSiS Lead Clinician.

4.2 Participants

Identifying appropriate patients and recruiting an adequate number of participants was essential to fulfil the clinical and statistical requirements.

4.2.1 Sample Size

The use of an intra-oral scanning device has not been used. Formal statistical support was provided by Dr W Wang, Institute of Motion Analysis and Research, University of Dundee. A sample size of 34 was determined to have a power of 80% to identify a clinically important difference of >1 GOSLON category at $p < 0.05$ between 2 model formats. As the data was to be collected for other studies (with further ethical approval and Caldicott Guardian approvals), it was decided to recruit up to 60 participants. It was noted that a minimum sample of 30 would be required to provide adequate power.

A minimum sample size of 16 respondents to the questionnaire would be required based on a clinical difference of 1 categorical point (standard deviation = 1.4), 80% power and $\alpha = 0.05$.

4.2.2 Inclusion/Exclusion Criteria

Potential participants attending Cleft Clinics in the Greater Glasgow & Clyde NHS Board area were identified from the CLEFTSiS (the National Managed Clinical Network for Patients with Clefts in Scotland) database. This required a data request form to be submitted to the Lead Clinician for approval and submission of all the necessary research approvals prior to extraction of any patient-identifiable information from the database. The study population were selected from the NHS Greater Glasgow and Clyde NHS Board area as this is the largest patient group in Scotland, accounting for approximately 40% of all new births with clefts each year.

Inclusion Criteria:

1. Subjects aged between 5 and 21 years of age
2. Unilateral cleft lip and palate

Exclusion Criteria

1. Any suspected or identifiable syndromes
2. Where they or their parents/carers were unable to provide assent/consent due to a lack of capacity.

4.2.3 Patient Information Sheets

Once identified as a potential participant a PIS and parent/carer information sheet was mailed along with the appointment card. The main body of the PIS outlined what to expect when attending as a participant for the study, the reasoning behind the study and the potential benefits of participating. Statements included in the PIS provided assurance of confidentiality and that participation was voluntary. The PIS included contact details should the participant or their parent/carer have had any questions regarding the study or any questions about participation in research in general. Details were also included for the contact person should there have been any problems experienced while participating or if there were any complaints.

Four versions of the PIS were created and approved by the co-sponsors and ethics service for language and content, and the age-appropriate PIS was sent. The three age groups for the PIS were age 5 (appendix II), 6-10 (appendix III) and 11-15 (appendix IV) and 16-21 (appendix V) A parent/carer information sheet (appendix VI) was also sent out to accompany the PIS for any potential participant under the age of 18.

4.3 Materials

4.3.1 Plaster Study Models

Upper and lower orthodontic impression trays (Ortho-Care (UK) Ltd) of an appropriate size were selected and filled with alginate (Exact Alginate, UnoDent Ltd, UK). The alginate was mixed using an automatic mixer (Pulsar MX-300 Alginate Mixer, Motion Medical Supplies & Equipment Corporation, Taiwan) to produce a reproducible consistency and setting time for the impression material.

Impressions of the maxillary and mandibular dentition were taken along with a wax occlusal registration with the patient occluding in maximum intercuspation. Any visibly inadequate impressions were repeated. The impressions and wax occlusal registration were submerged in disinfectant solution (Perform 1D Schülke & Mayr Ltd, UK) for decontamination for 10 minutes prior to being transported to the Orthodontic Laboratory. A single member of the research team took the impressions (TG).



Figure 26 Impression trays.



Figure 27 Pulsar MX-300 Alginate Mixer

Plaster study models were poured from the impression in 100% dental stone (Yellow Stone, John Winter & Co Ltd, UK) and the bases trimmed corresponding to the occlusal registration. The models were anonymised and allocated a subject number.

4.3.2 Direct Study Models

Following a training session, the maxillary and mandibular dental arches were then scanned separately and in occlusion using an intraoral 3D scanner [Trios® Digital Impressions Scanner € (3Shape A/S, Copenhagen, Denmark)] to produce direct digital models utilising optical sectioning technology. Any areas of the dentition that were not adequately scanned were repeated until the investigator was satisfied with the quality of the scan. A single member of the research team undertook the intra-oral scanning (EC).



Figure 28 Trios digital impression scanner

4.3.3 Indirect Study Models

Anonymised plaster study models were taken by one investigator (EC) to ESM Digital Solutions in Dublin for 3D scanning. The plaster models were scanned by a 3D scanner [R700 Orthodontic Study Model Scanner€ (3Shape A/S, Copenhagen, Denmark)] to create indirect digital study models using laser scanning technology (see section 2.12.3).



Figure 29 R700 orthodontic model and impression scanner.

4.3.4 Questionnaire

Prior to commencing the study no previous questionnaire had been used to compare patients' experiences of having dental impressions and intra oral scans taken. Therefore, a participant questionnaire (appendix VII) was constructed with a Flesch Reading ease of 70.1 and Flesch-Kincaid Grade level of 7.6 indicating a reading age of 11. Any participants aged 11 or under could be assisted by their parent or guardian to complete the questionnaire. A similar questionnaire (appendix VIII) was created to obtain feedback from the parent/carer.

Both questionnaires were approved by the co-sponsors and ethics committee.

Using a categorical scale, the participant questionnaire invited the subject to score their perceptions and time required for the routine dental impression and the same domains for the 3D scan. The scoring was from 'Very Good' (1), 'Good' (2), 'OK' (3), 'Bad' (4) to 'Very Bad' (5). The option to say 'I don't know' (X) was also provided.

The parent/carer questionnaire used an identical scoring system and asked them to score their views on their child's experience of having a routine dental impression and a 3D scan carried out. Both questionnaires were issued by an investigator and were completed without the investigator being present to avoid any influence.

4.4 Methods

The outline of the methods is shown in Figure 30.

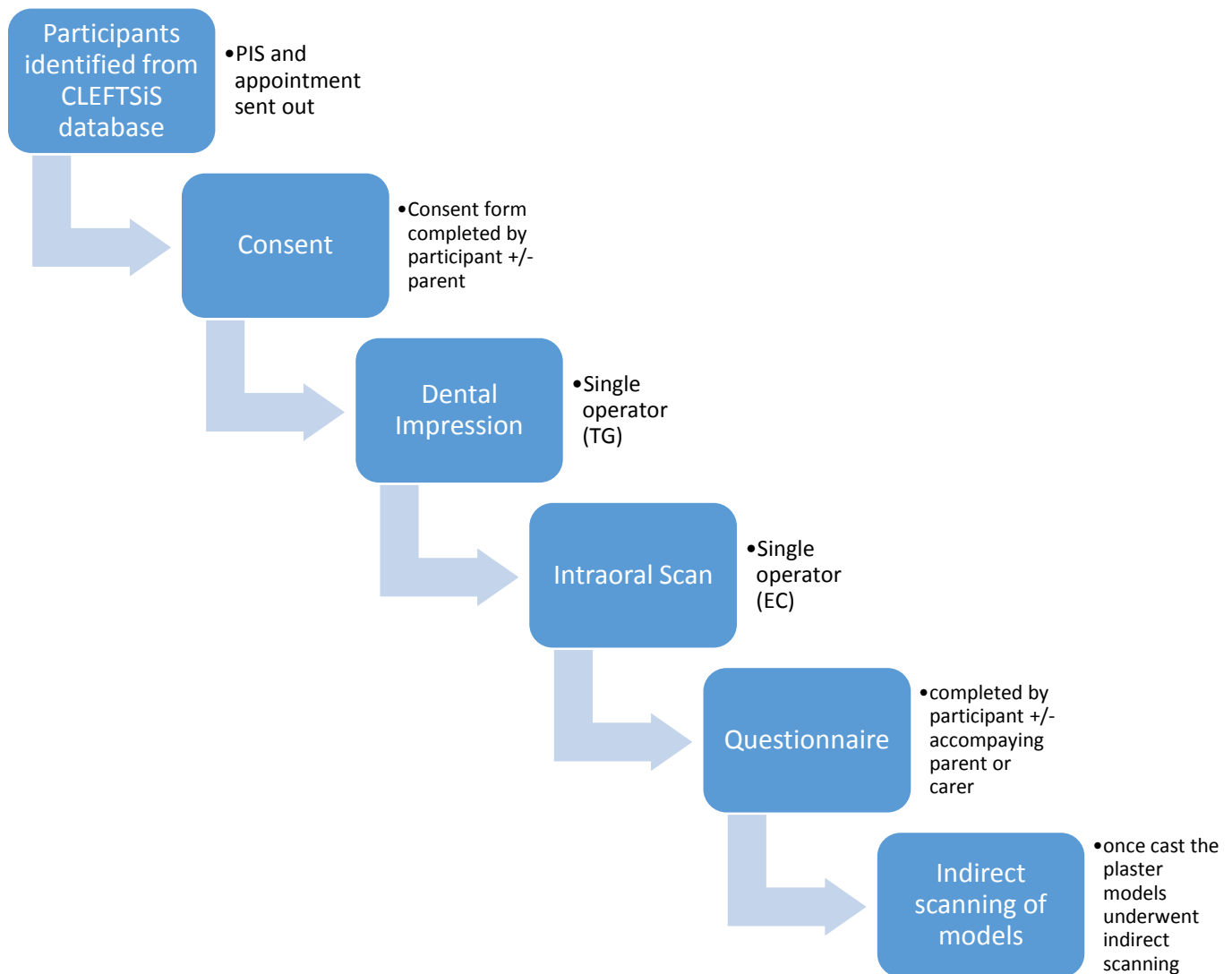


Figure 30 Outline of methodology.

4.4.1 Clinical Procedure

On attending the clinic with their parent/carer, the procedure was explained by one of the Research Team (CM) and they were offered the opportunity to ask any questions. Written consent was obtained by one of the members of the research team (EC). A participant consent form (appendix IX) was completed for all subjects aged over the age of 5. An assent form (appendix X) was available for any participants aged 5. Written consent was obtained from the parent/guardian (appendix XI) and they were also asked to counter sign the participant consent form.

On entering the clinic the participant was asked to sit in the dental chair and the parent/guardian was invited to sit in a chair within the surgery. Impressions of the maxillary and mandibular dental arches were taken for the construction of study models and cast in plaster. The dental impressions were taken by a single member of the Care Team (TG). The dental arches were then be scanned separately and in occlusion using an intraoral 3D scanner [Trios® Digital Impressions Scanner[€] (3Shape A/S, Copenhagen, Denmark)] to produce direct digital models (B). The intra oral scanner was on loan from ESM Digital Solutions (Dublin, Ireland) for the duration of the data collection. The intraoral scanning was carried out by a single member of the research team (EC).

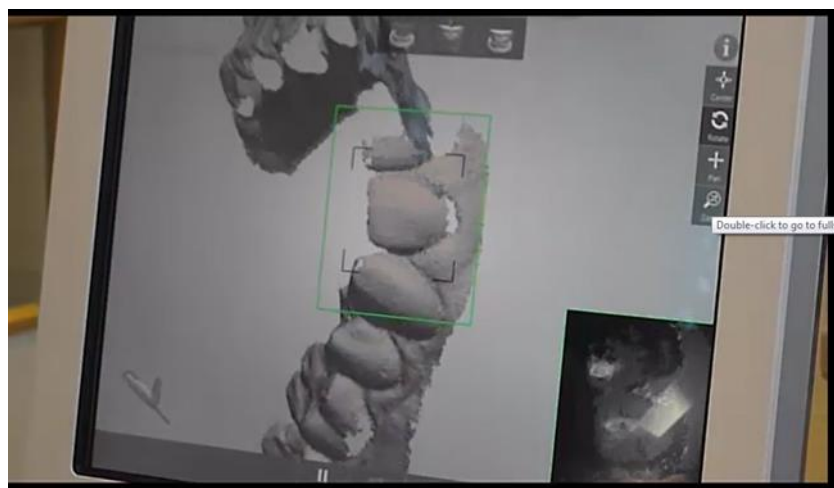


Figure 31 Trios screen display during scanning.

The participant and their parent/guardian were then asked to complete a simple questionnaire (appendix VII and VIII) about their experiences of having dental impressions and the 3D scan. The questionnaire was explained to the participant and parent/carer by a member of the Research Team and the opportunity to ask any questions was given.

The plaster models were scanned by a 3D scanner [R700 Orthodontic Study Model Scanner[€] (3Shape A/S, Copenhagen, Denmark)] to create indirect digital study models (C). Anonymised plaster study models were taken by a member of the research team (EC) to ESM Digital Solutions in Dublin to undergo 3D scanning. The models were orientated into the correct occlusion and held in this position with a scanning jig.



Figure 32 Occlusal jig.

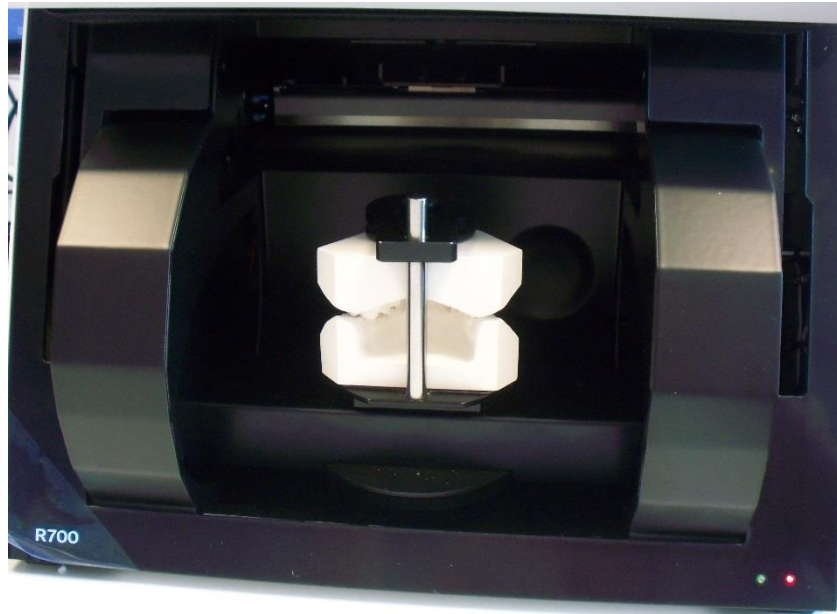


Figure 33 Models mounted onto jig and placed in R700 Scanner.

4.5 Examiners

Three Orthodontic Consultants experienced in cleft care, one from Glasgow Dental Hospital and two from Dundee Dental Hospital, examined and scored the plaster, direct and indirect models. All examiners had previously undergone calibration for the GOSLON yardstick and were competent in the use of the MHB index. All three examiners use both the GOSLON and MHB indices in routine clinical practice.

4.6 Model Scoring

All formats of the study models were scored on 2 separate occasions at least one month apart to eliminate memory bias (Figure 34). The GOSLON reference models were available throughout the scoring process.

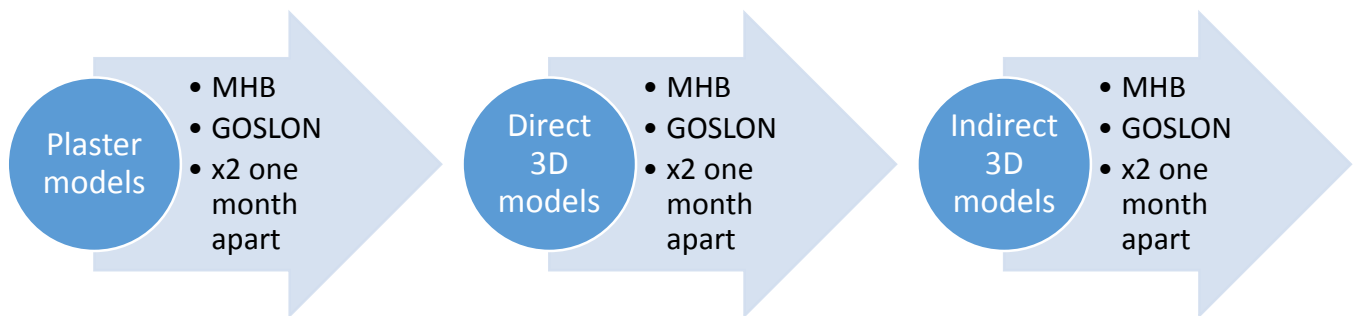


Figure 34 Model scoring process.

Scoring of the plaster models took place in a lecture theatre with the models set out in a random order. Data was collected on a scoring sheet (appendix XII) and then entered into a spread sheet (Excel, Microsoft, California, USA).




Figure 35 Plaster model scoring in lecture theatre.

Plaster Study Model Scoring Round 1

Examiner: PM

Subject number: 19



Goslon Index: Score 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐

Huddart & Bodenham Score:

Right Buccal Segment				Labial Segment		Left Buccal Segment			
6	E	D	C	1	1	C	D	E	6
+3	-3	-3	-3	-3	-3	-3	-3	-3	-3
-2	-2	-2	-2	-2	-2	-2	-2	-2	-2
-1	-1	-1	-1	-1	-1	-1	-1	-1	-1
0	0	0	0	0	0	0	0	0	0
+1	+1	+1	+1	+1	+1	+1	+1	+1	+1
Sum: <input type="text"/>				Sum: <input type="text"/>		Sum: <input type="text"/>			
TOTAL SUM: <input type="text"/>									

Figure 36 Model with scoring sheet.

Scoring of the direct and indirect 3D models was undertaken on a lap top with 13.3" Backlit LED HD (1366x768) resolution display using orthodontic 3D study model imaging software [3Shape OrthoAnalyzer™ Software (3Shape A/S, Copenhagen, Denmark)]. The models could be orientated into standard positions of front view, rear view, right side view, left side view and open mouth view. The examiner was able to rotate the model freely and zoom in and out by using the mouse.

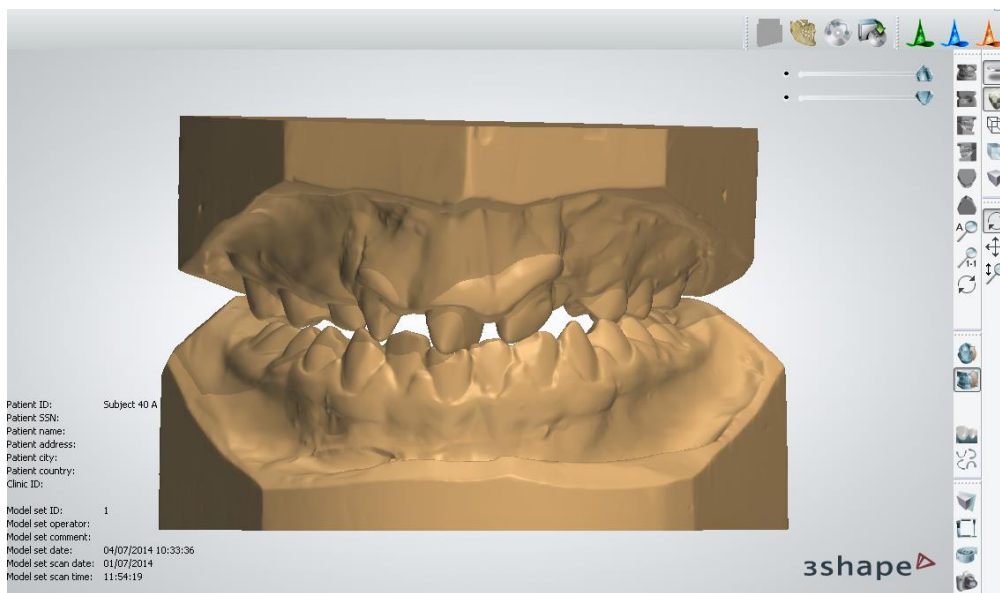


Figure 37 Front view.

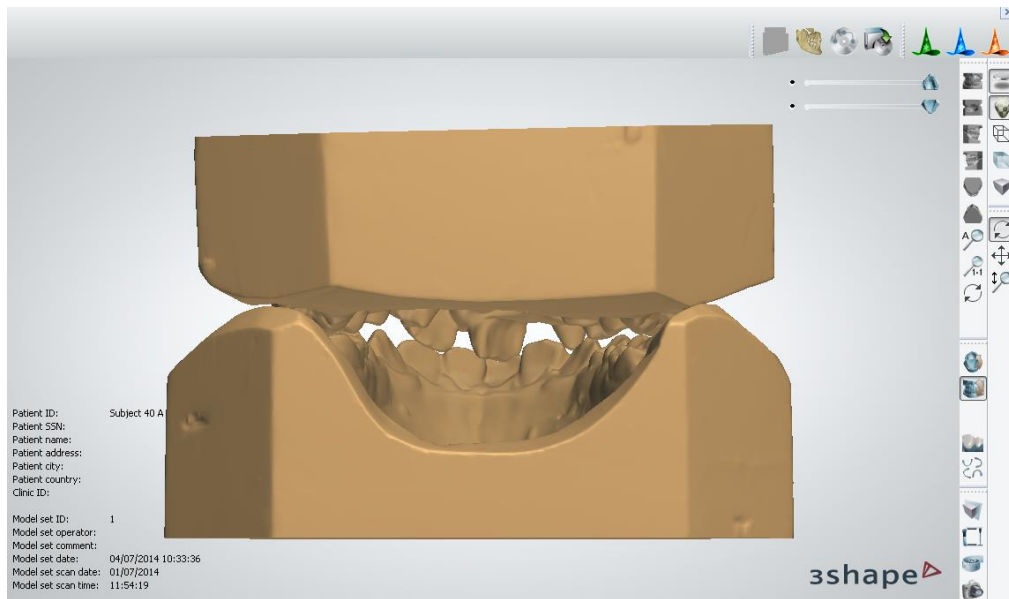


Figure 38 Rear view.

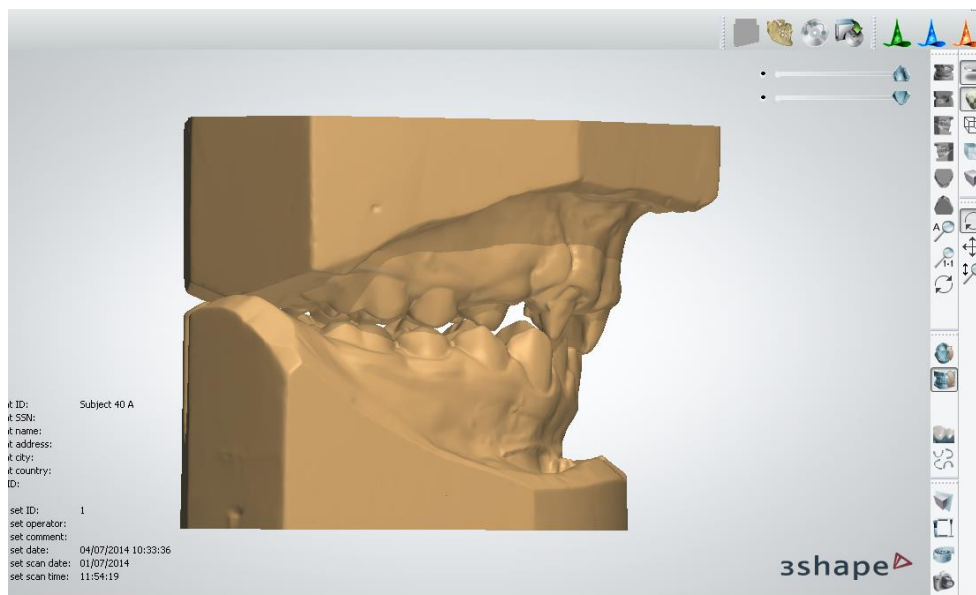


Figure 39 Right side view.

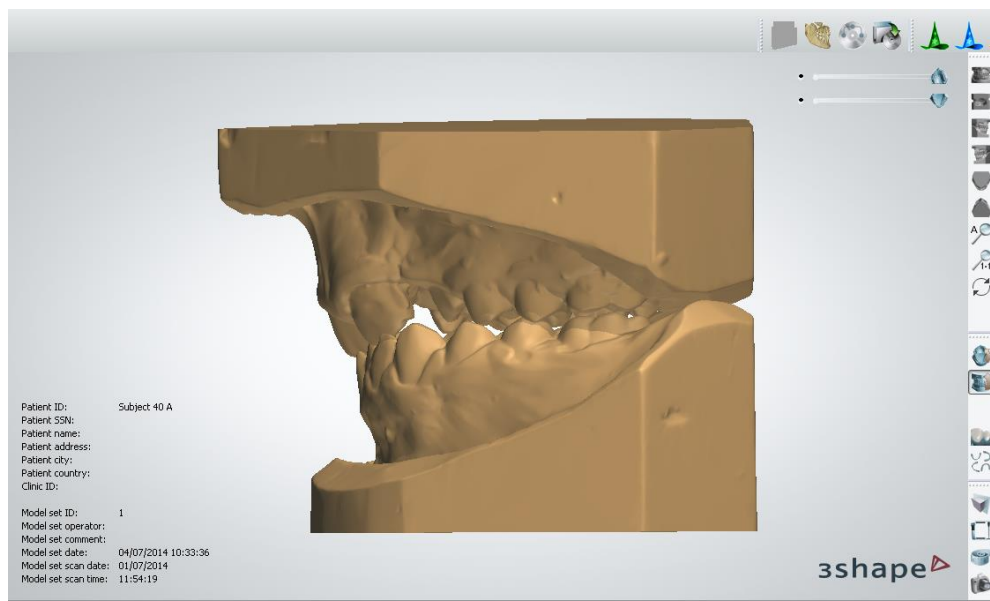


Figure 40 Left side view.

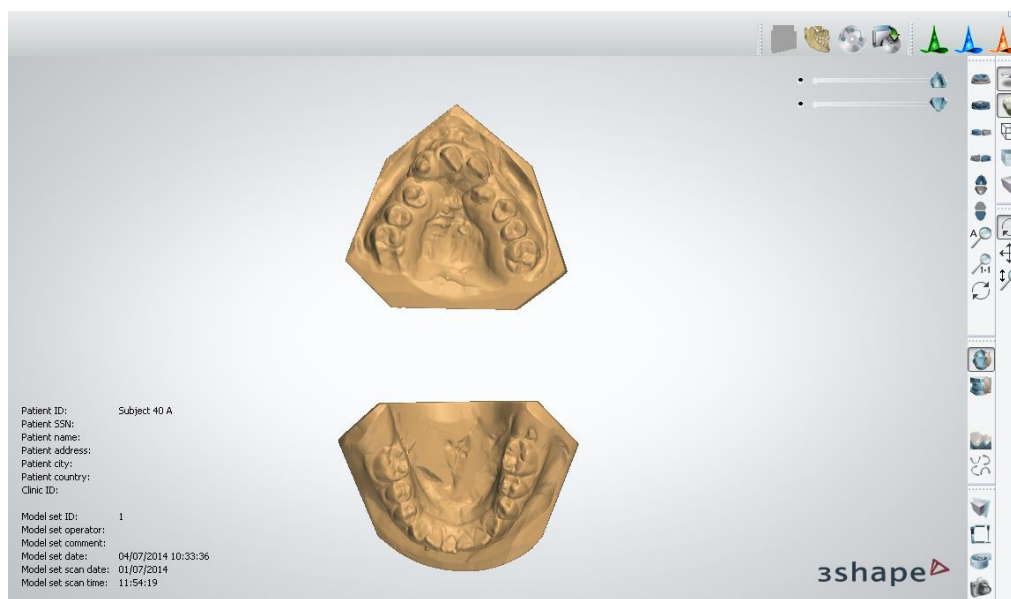


Figure 41 Open mouth view.

4.5 Statistical Analysis

Descriptive statistics were used to describe the demographics of the sample.

Both the MHB and GOSLON are both scalar measurements of surgical outcome in cleft lip and palate. The MHB is a continuous scale of severity in comparison to the GOSLON which is a categorical scale.

Items within a scale are required to have internal consistency. 'The items should measure the same thing, so they should be correlated with each other' (Bland and Altman 1997, Kaplan and Saccuzzo 2009).

Intra-class correlation coefficients (ICC), e.g. Cronbach's alpha model, measure internal consistency or measurement reliability and can be used in multipoint formatted questionnaires or scales. ICC is expressed as a number between 0 and 1. An increasing value of ICC is given when items scored are correlated with each other. For comparing groups an ICC value of between 0.7 and 0.8 is regarded as acceptable for preliminary and basic research and 0.9-0.95 for applied research (Table 7) (Bland and Altman 1997, Kaplan 1982, Nunnally 1978).

Author	Situation	Recommended Level
(Kaplan 1982)	Basic research Applied research	0.7-0.8 0.95
(Nunnally 1978)	Preliminary research Basic research Applied research	0.7 0.8 0.9-0.95

Table 7 Recommended reliability levels. Adapted from Peterson (1994).

The GOSLON and MHB scores for each medium of study model were uploaded into IBM SPSS Statistics software version 21.0 (IBM Corporation, New York, USA). The ICC analysis was performed to determine inter-examiner reliability.

Inter-examiner reliability was assessed using Bland Altman plots for the MHB data with the data being tested for each model medium using a one-sample T-test ($P < 0.05$). The questionnaire data were statistically tested using Wilcoxon signed ranks tests ($p < 0.05$).

CHAPTER FIVE: RESULTS

5.1 Subjects' Demographics

In total 46 patients were recruited to the study (Figure 42). Twenty five (54%) of the subjects were female and 21 (46%) were male. The age range of subjects was from 9 to 21 (Figure 43). When it came to having the dental impressions taken in the clinic 3 patients declined but had undergone direct scanning of their dentition. The demographics of those who withdrew were as follows: 15 year old female, 14 year old female and 9 year old female.

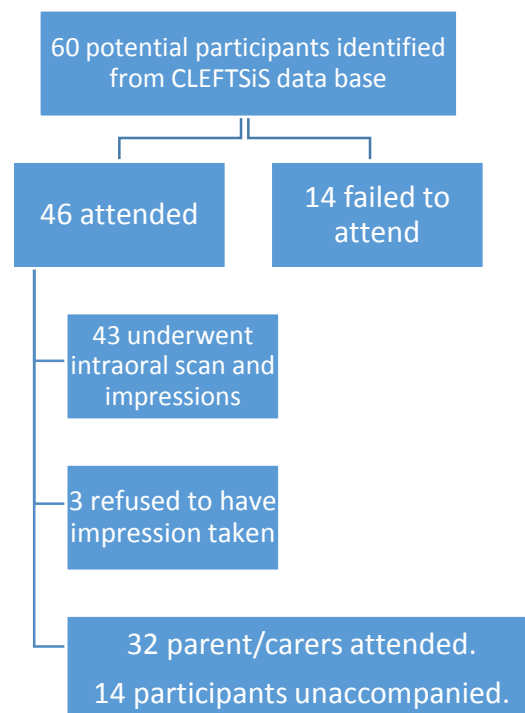


Figure 42 Participant recruitment.

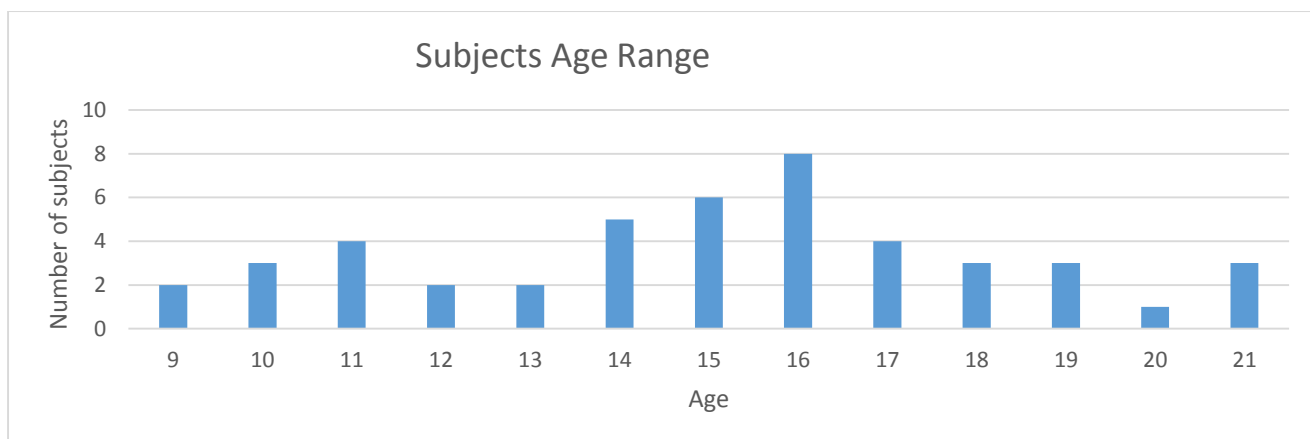


Figure 43 Subjects age range (n=43).

5.2 Examiner reliability

The ICC analysis (Cronbach's Alpha model) was performed (Table 8). Each medium of study model was scored $\alpha > 0.98$. All examiners also achieved a reliability score greater than 0.98 which is deemed to be above the acceptable range for clinical application. From the ICCs examiner 3 showed the highest intra-examiner reliability (Table 9).

Reliability Statistics				
method	Cronbach's Alpha	95% Confidence Interval		N of Items
		Lower bound	Upper bound	
plaster	.988	.986	.989	2
direct	.990	.989	.992	2
indirect	.984	.981	.986	2

Table 8 Internal consistency of study model mediums.

Reliability Statistics

Consultant	Cronbach's Alpha	95% Confidence Interval		N of Items
		Lower bound	Upper bound	
1	.986	.984	.988	2
2	.985	.983	.987	2
3	.991	.990	.992	2

Table 9 Intra-examiner reliability.

To visualise the differences of the MHB scores made by the examiners Bland Altman plots were created, plotting the differences of the bias (Y-axis) versus the mean of the MHB scores (X-axis).

5.2.1 Plaster models

The mean difference for MHB scoring of plaster models was found to be 0.0930 with a standard deviation of 2.14491. There was no statistically significant difference between 0 and the mean difference in the measurements ($p=0.623$) (Table 10).

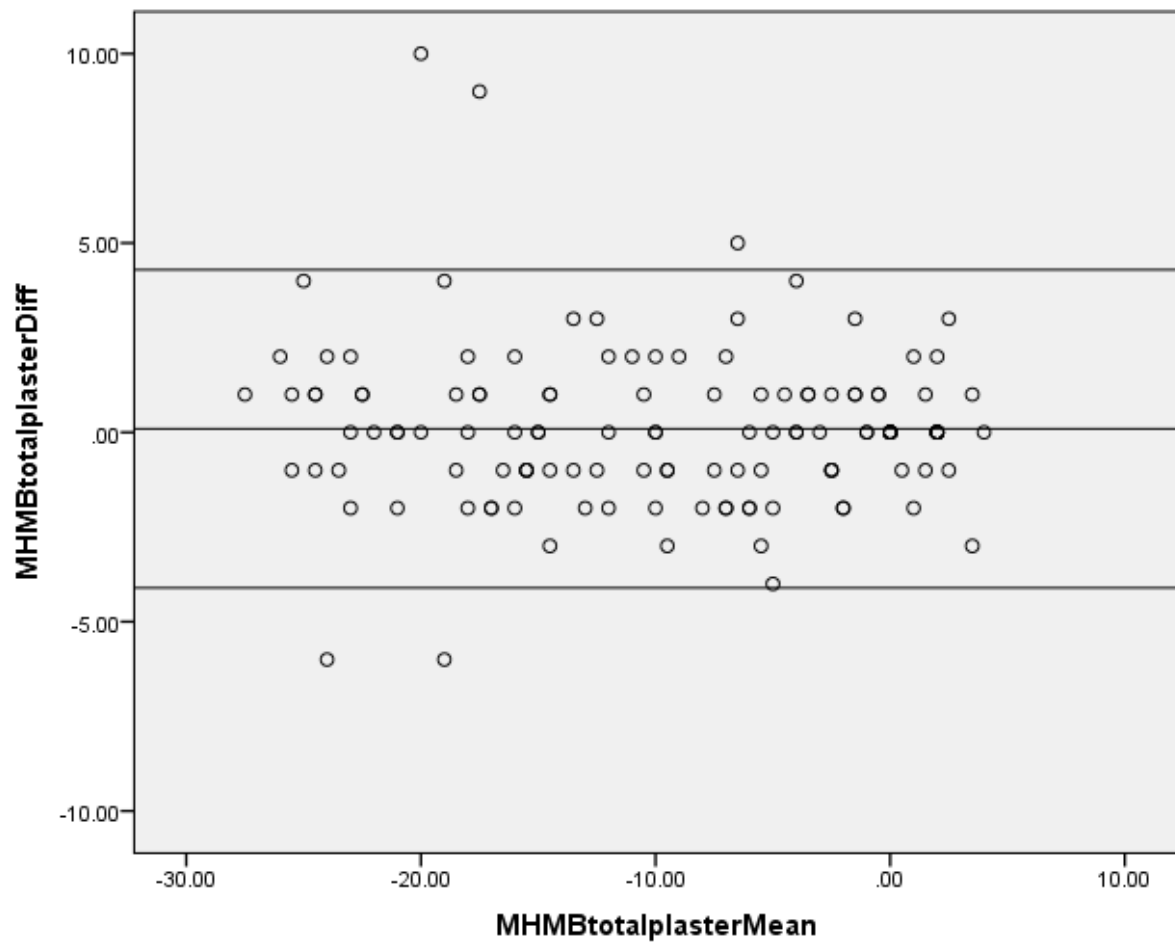


Figure 44 Bland Altman plot of MHB scoring of plaster models.

One-Sample Statistics

	N	Mean	Std. Deviation	Std. Error Mean
MHB total plaster Diff	129	.0930	2.14491	.18885

One-Sample Test

	Test Value = 0					
	t	df	Sig. (2-tailed)	Mean Difference	95% Confidence Interval of the Difference	
					Lower	Upper
MHB total plaster Diff	.493	128	.623	.09302	-.2806	.4667

Table 10 T test of MHB scoring of plaster models.

5.2.2 Indirect Digital Models

The mean difference for MHB scoring of indirect 3D digital models was found to be 0.1318 with a standard deviation of 1.98581(Figure 45). There was no statistically significant difference between 0 and the mean difference in the measurements ($p=0.452$) (Table 11).

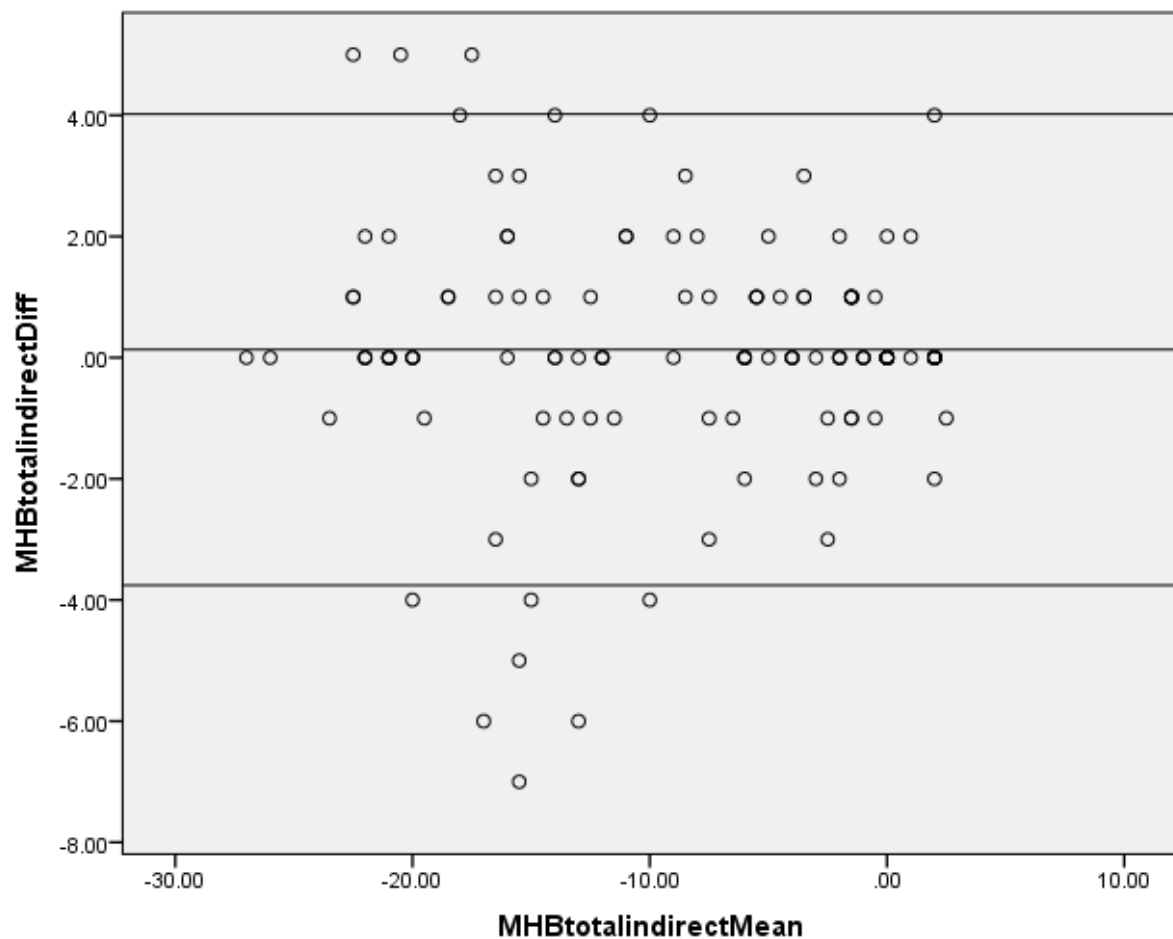


Figure 45 Bland Altman plot of MHB scoring of indirect 3D digital models.

One-Sample Statistics

	N	Mean	Std. Deviation	Std. Error Mean
MHB total indirect Diff	129	.1318	1.98581	.17484

One-Sample Test

	Test Value = 0					
	t	df	Sig. (2-tailed)	Mean Difference	95% Confidence Interval of the Difference	
					Lower	Upper
MHB total indirect Diff	.754	128	.452	.13178	-.2142	.4777

Table 11 T test of MHB scoring of indirect 3D digital models.

5.2.3 Direct Digital Models

The mean difference for MHB scoring of indirect 3D digital models was found to be 0.0155 with a standard deviation of 1.72294 (Figure 46). There was no statistically significant difference between 0 and the mean difference in the measurements ($p=0.919$) (Table 12).

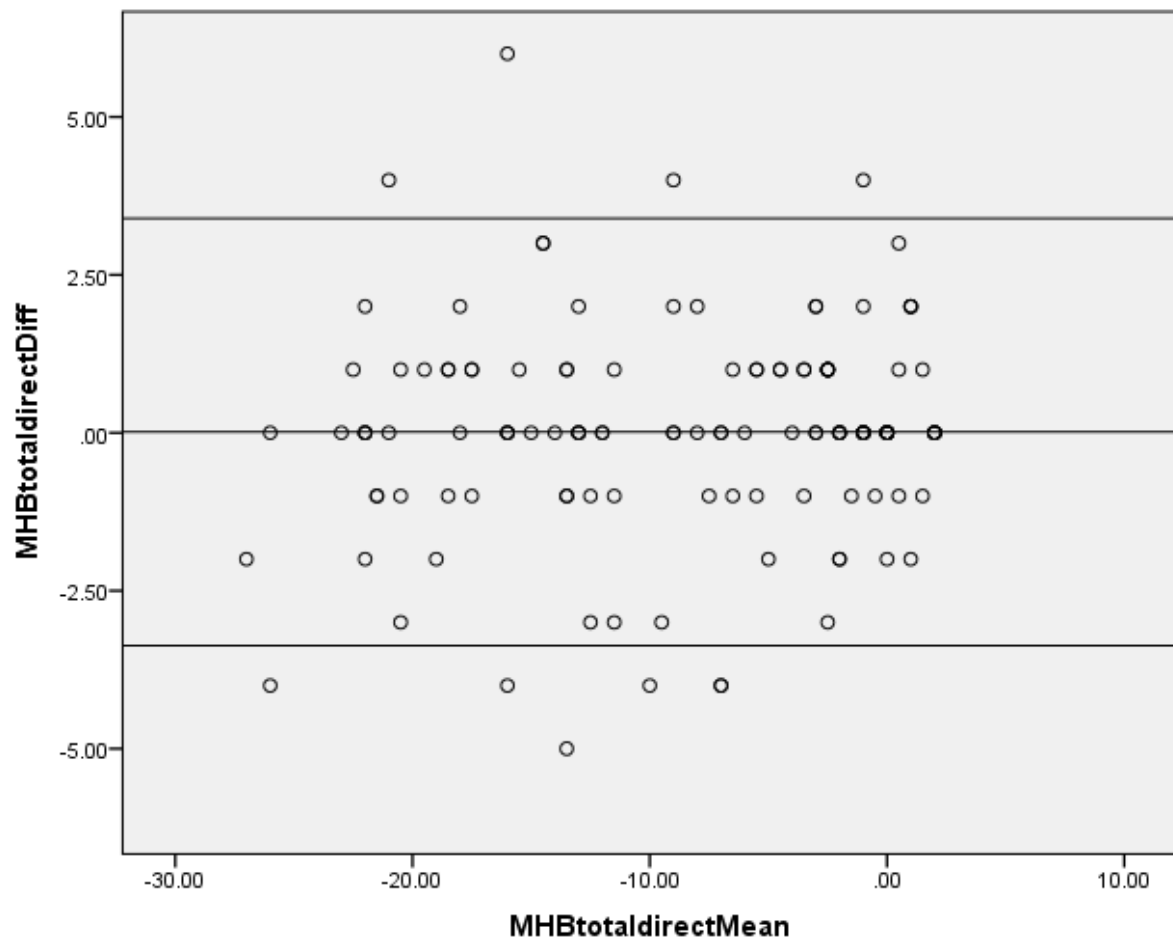


Figure 46 Bland Altman plot of MHB scoring of direct 3D digital models.

One-Sample Statistics

	N	Mean	Std. Deviation	Std. Error Mean
MHB total direct Diff	129	.0155	1.72294	.15170

One-Sample Test

	Test Value = 0					
	t	df	Sig. (2-tailed)	Mean Difference	95% Confidence Interval of the Difference	
					Lower	Upper
MHB total direct Diff	.102	128	.919	.01550	-.2847	.3157

Table 12 T test of MHB scoring of direct 3D digital models.

5.3 Questionnaire

All 43 of the study participants completed a questionnaire after taking part in the study. The 3 participants who refused to have a routine alginate impression taken did not complete the questionnaires.

5.4 Participant feedback

5.4.1 Impressions

Participants who underwent the impression taking were asked to score their experiences as 'Very Good' (1), 'Good' (2), 'OK' (3), 'Bad' (4) to 'Very Bad' (5) and the option to say 'I don't know' (X) was also given.

The first question asked the patient to reflect on their experience of how the routine impression felt (Figure 47). 44.2% felt it was good or very good and 39.5% felt it was OK. 16.3% felt it was a negative experience rating their experience as bad or very bad.

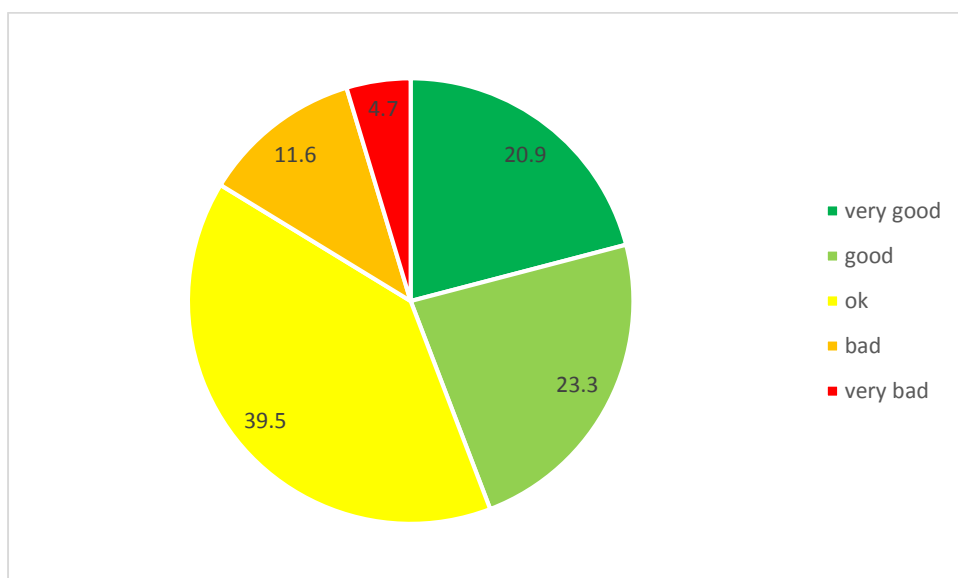


Figure 47 Participants: impression experience.

The second question focussed on how the participant felt about the time taken to have an impression taken (Figure 48). Just over half of the participants (51.2%) found the time taken to have impressions to be positive (good or very good) and 13.9% gave a negative reflection (bad or very bad).

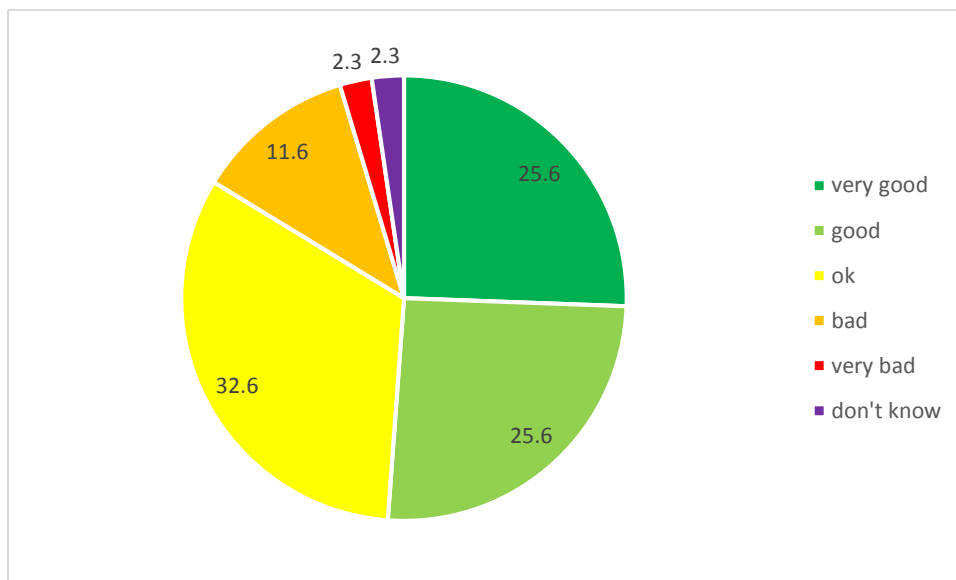


Figure 48 Participants: impression time taken.

5.4.2 3D scan.

The participants were then asked to score their experience of the 3D scanner both in regards to the time taken and how it felt (Figure 49 & Figure 50). No participants found the 3D scanner to be a negative experience in regards to how it felt. The majority (56.6%) of patients found the time taken to have the 3D scan carried out was good or very good. A similar negative feedback for the time taken was found for routine impressions vs the 3D scan (16.3% vs 15.2%).

Participants significantly preferred how the 3D scan felt ($p < 0.00018$) but there was no significant difference in regards to time taken (Table 13).

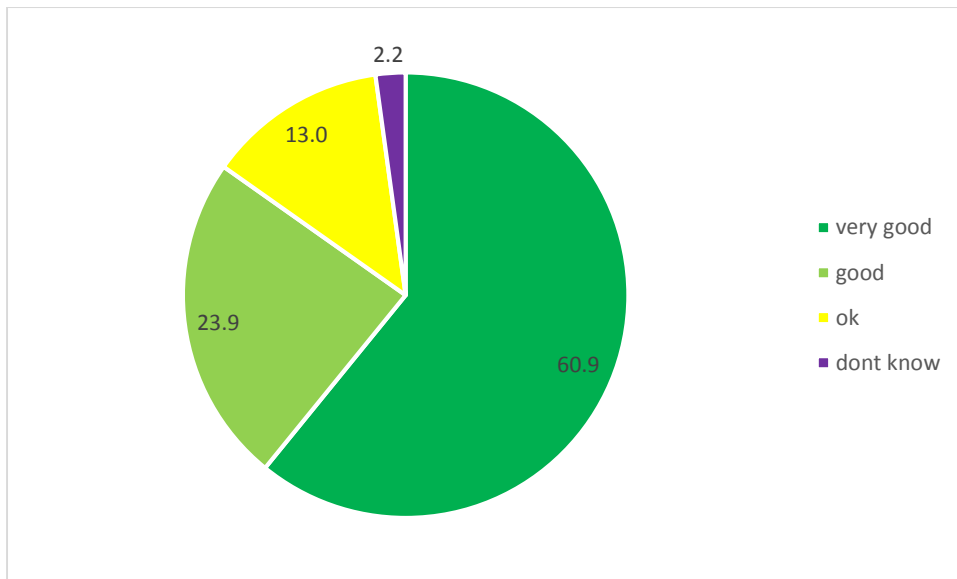


Figure 49 Participants: 3D scan experience.

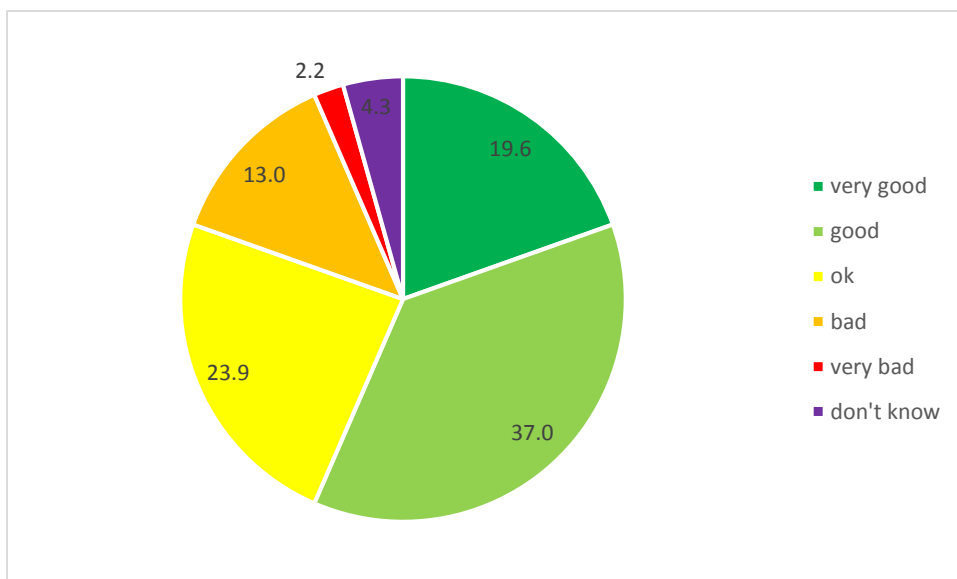


Figure 50 Participants: 3D scan time taken.

5.5 Parent/Carer feedback

5.5.1 Impressions

Thirty-two accompanying parents/carers attended with the participants. 14 participants were unaccompanied. Only one parent/carer completed a questionnaire per participant. The format was very similar to the participant questionnaire, they were asked to score how they felt their child's experience of the routine impressions and 3D scan had been from 1-5 ('Very Good' (1), 'Good (2), OK (3), Bad (4) to 'Very Bad'(5) and the option to say 'I don't know' (X)).

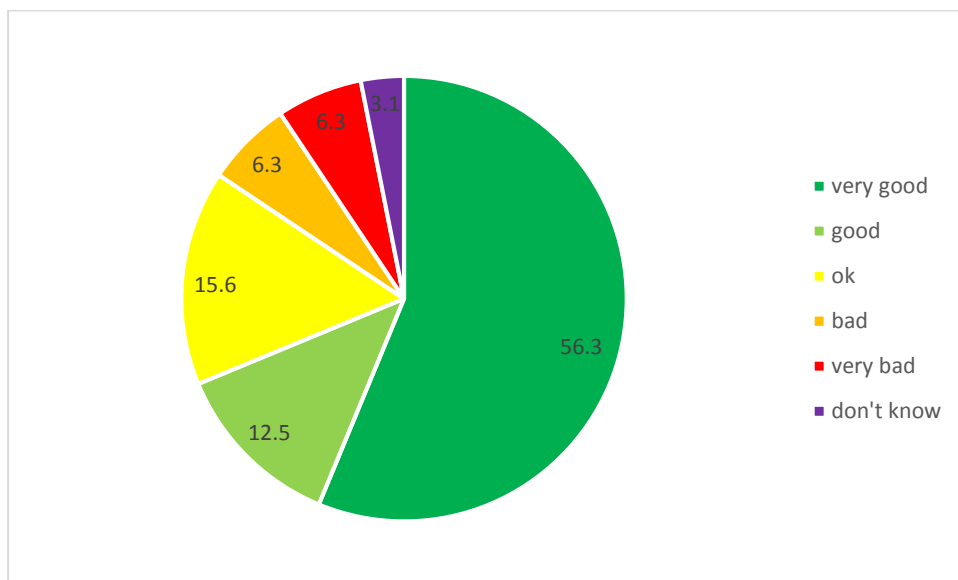


Figure 51: Parent/carer feedback: impression experience.

The parents' evaluations of their child's experience of dental impressions were generally positive (68.8% how it felt and 75% time taken) with 12.6% reporting a negative experience (Figure 51 & Figure 52).

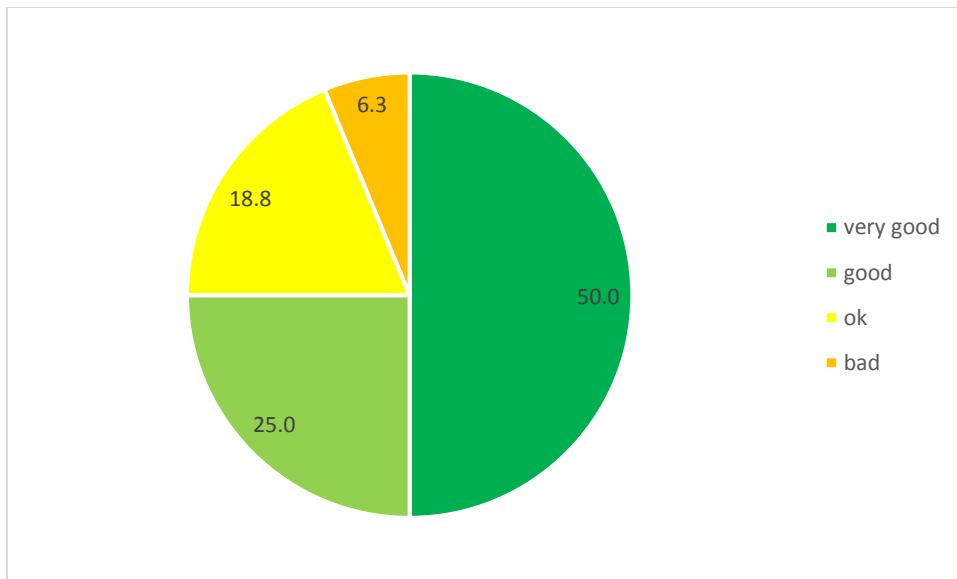


Figure 52 Parent/carer feedback: impression time taken.

5.5.2 3D scan

There was no negative feedback given by accompanying parents/carers in regards to their child's experience of the 3D scanner (Figure 53 & Figure 54). The parents/carers significantly preferred their child experiences of the 3D scanner in comparison to the routine impressions in regards to how it felt ($p < 0.003$) and the time taken ($p < 0.030$) (Table 13).

Test Statistics

	Children 3D scan felt – Children Impression felt	Children 3D scan time – Children Impression time	Parent 3D scan felt – Parent Impression felt	Parent 3Dscan time – Parent Impression time
Asymp. Sig. (2- tailed)	.000	.536	.003	.030

Table 13 Wilcoxon Signed Ranks Test results for the questionnaire.

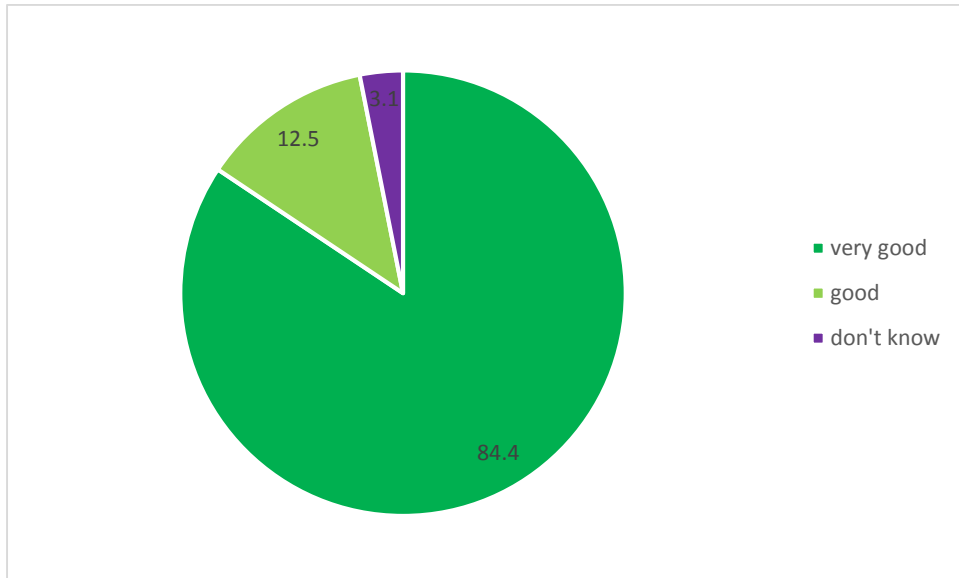


Figure 53 Parent/carer feedback: 3D scan experience.

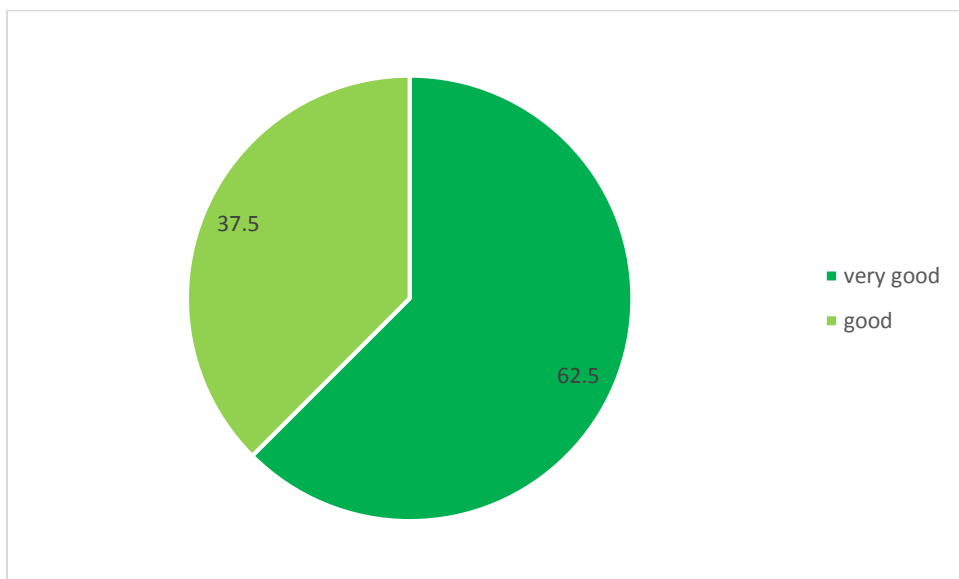


Figure 54 Parent/carer feedback: 3D scan time taken.

CHAPTER SIX: DISCUSSION

6.1 Results

The scoring of 3D digital models from intraoral scanning was found to be more reliable and reproducible than plaster models for the assessment of dental arch relationships in UCLP.

Intra- and inter-observer reliability were good and both the subjects and their parent/carer expressed a preference for intra-oral scanning over traditional impressions. These findings are discussed below.

6.1.1 Examiner Reliability

All three examiners were found to have Cronbach's Alpha reliability scores greater than 0.98 for each study model medium (plaster, indirect and direct) which is been deemed to be above the acceptable threshold for clinical applications by a number of authors (Bland and Altman 1997, Kaplan 1982, Nunnally 1978). This indicates that the GOSLON and MHB scoring carried out on plaster, indirect and direct study models had an acceptable internal consistency and good intra-examiner reliability.

Inter-examiner reliability was assessed using Bland Altman plots for the MHB data. The direct digital scans demonstrated superior inter-examiner reliability than indirect digital scans, which in turn was greater than that for the 'gold standard' plaster models (which was nevertheless acceptable). The null hypothesis was therefore rejected as direct digital study models were shown to have higher reliability than plaster study models.

These results demonstrate that plaster, indirect and direct digital study models are all reliable and reproducible for scoring treatment outcomes GOSLON and MHB for patients

with UCLP. As the reliability of the data obtained using direct digital models was superior to that obtained from the current 'gold standard' of plaster models, it would be reasonable to recommend that intra-oral scanning could replace routine impression taking for recording the occlusion for the assessment of surgical outcomes in UCLP.

The use of direct intra-oral scanning for this purpose has not previously been published at the time of writing and therefore no comparative data was available. The literature includes several studies comparing the current practice of creating plaster study models versus 2D imaging with photographs (Table 14) and indirect 3D digital study models (Table 15).

Authors	Methods	Cleft Type	Sample size	Index/Indices/ Measurements Used	Findings
(Nollet <i>et al.</i>, 2004)	Plaster models vs photographs plaster models Retrospective records 4 examiners	UCLP	n=49	GOSLON	Intra-observer agreement (mean Pearson reliability coefficient): plaster 0.83, photographs 0.87. Inter- and intra-examiner reliability (weighted kappa): Inter-examiner agreement: Plaster 0.76, photographs 0.70. Intra-examiner agreement between photograph and plaster models: 0.75. GOSLON rating with the use of photographs is a consistent, reproducible.
(Ali <i>et al.</i>, 2006)	Plaster models vs digital photographs of study models Retrospective records 3 examiners	UCLP	n=56	MHB OJ	Inter- and intra-examiner reliability (weighted kappa): Mean kappa for MHB from photographs: 0.65 (± 0.05) Mean kappa for OJ from photographs: 0.68 (± 0.07) Inter-examiner values ranged from 0.64 to 0.71. Altman (Altman 1991) suggests this shows good agreement using photographs.
(Liao <i>et al.</i>, 2009)	Plaster models and digital intraoral photographs Retrospective records 4 examiners	UCLP	n=58	GOSLON	Agreement between photograph and plaster model rating (weighted kappa): 0.93 to 0.97. Inter and intra-examiner agreement on photographs (weighted kappa): 0.86 to 0.99.No significant difference between the rating of plaster models and photographs
(McAuliffe <i>et al.</i>, 2010)	Plaster study models vs intraoral photographs. Retrospective records 4 examiners	UCLP	n=96	5-year-olds' index	Inter and intra-examiner agreement (weighted kappa): Intra-examiner agreement: plaster 0.54 to 0.85, photographs 0.60 to 0.82.Inter-examiner agreement: plaster 0.57, photographs 0.46. Overall inter-examiner agreement was moderate for both study models and photographs.

Table 14 Cleft surgical outcome scoring from 2D images.

Authors	Methods	Cleft Type	Sample Size	Index/Indices Used	Findings
(Leenarts <i>et al.</i> , 2012)	Plaster vs photographs vs digital models. Retrospective records 4 examiners	BCLP	n=20	BCLP Yardstick	Inter and intra-examiner agreement (weighted kappa): Intra-examiner agreement: 0.692 to 0.885. Inter-examiner agreement: 0.756 to 0.8. No significant differences were found for the BCLP yardstick scores among the three formats.
(Asquith and McIntyre, 2012)	Plaster vs indirect study models Retrospective records R250 scanner 3 examiners	UCLP	n=30	5-year-olds' index MHB	Inter and intra-examiner agreement (weighted kappa): Intra-examiner agreement: 0.62 to 0.83. Inter-examiner agreement: 0.64 to 0.78. No statistically significant differences between the scores for the 3D digital study models when compared to the plaster study models for either the 5-year-olds' index ($p = 0.12$) or for the modified Huddart Bodenham index ($p = 0.506$).
(Servet <i>et al.</i> , 2012)	Plaster models vs photographs of plaster models vs indirect 3D digital models Retrospective records 2 examiners	UCLP	n=70	GOSLON	Inter and intra-examiner agreement (weighted kappa): Intra-examiner agreement: 0.86 to 0.96 Inter-examiner agreement: 0.81 to 0.96. GOSLON scoring on 2D and 3D images showed high reliability when compared with the dental casts for rating the dental arch relationships of patients with UCLP.
(Chawla <i>et al.</i> , 2013)	Plaster models vs indirect 3D digital models Retrospective records R640 Scanner 3 examiners	UCLP	n=45	5-year-olds' index	Inter-examiner agreement (weighted kappa): Plaster models: 0.83 to 0.87 Indirect 3D digital models: 0.74 to 0.83. 3D indirect digital models are a reproducible and reliable alternative to plaster models for rating dental arch relationships using the 5-year-olds' index.

Table 15 Cleft surgical outcome scoring from 3D images.

Previous investigations of the reliability of surgical outcome measures on new methods of archiving study models have used Cohen's weighted kappa analysis to calculate inter- and intra-examiner reliability (Gray and Mossey 2005, MARS *et al.*, 1992, Mossey *et al.*, 2003, Noverraz *et al.*, 1993).

The degree of agreement of kappa has been described by Altman (Altman 1991) and is outlined in Table 16.

Kappa (k) Value	Strength of Agreement
0.20	Poor
0.21-40	Fair
0.41-0.60	Moderate
0.61-0.80	Good
0.81-1.00	Very Good

Table 16 Level of agreement using weighted kappa (k) values (Altman, 1991).

Intra-examiner reliability within the literature for indirect 3D digital models ranges from 0.62 to 0.96 and inter-examiner reliability ranges from 0.64 to 0.96 (Table 15). This corresponds to 'good' to 'very good' strength of agreement (Altman 1991). The findings from this study regarding the reliability of indirect 3D digital models in cleft care are therefore in keeping with the current literature as all three examiners scored the indirect 3D digital models above the threshold for acceptable internal consistency indicating that cleft care outcomes (GOSLON and MHB) can be reliably assessed on digital models.

This study found that the reliability of scoring using two different indices on 3D intra-oral scans was superior to that of both indirect digital models and plaster models and 3D intra-oral scans could therefore replace indirect digital and plaster models for the assessment of dental arch relationships in cleft care.

6.1.2 Questionnaire

The secondary aim of this project was to obtain patient and parent/carer feedback regarding the experience of having routine impressions and intra-oral scans. Patient feedback is increasingly being considered in healthcare but has had limited attention in cleft care outcome studies (Turner *et al.*, 1997). Of these, the CSAG and Eurocleft studies both included parent and patient satisfaction about the organisation and quality of cleft care (Semb *et al.*, 2005, Williams *et al.*, 2001).

Patient feedback is an important element in the potential introduction of an alternative diagnostic or therapeutic technique such as that for recording occlusal relationships. If there is negative feedback in comparison to the currently practiced impression technique the replacement with an intra-oral scanner is likely to be poorly tolerated no matter how accurate it may be found to be.

The patient feedback regarding routine dental impressions was mixed both in regards to how it felt and the time taken with patients scoring from (1) very good to (5) very bad. In comparison, the feedback for the intra-oral scan indicated a more positive response to 'how it felt' and it was shown that participants strongly preferred having a 3D scan ($p=0.00018$). There was no significant difference in regards to the perception of the time taken for either the impression or scan ($p>0.535$).

The feedback obtained by Yuzbasioglu *et al.*, (2014) was highly supportive of intra-oral scanning as 100% of 1st year medical and dental students who underwent routine impressions and an intra-oral 3D scan (Cerec OMNICAM, Sirona Dental GmbH, Wals Bei Salzburg, Austria) preferred the new technique. A 9-item comparative questionnaire was used to obtain feedback (Figure 55)

Preferences	Conventional	Digital
Which impression technique do you prefer in case of one more time for impression procedure?	%0	%100
Which impression technique is more comfortable from point of comparison of two impression procedure?	%0	%100
Which impression technique do you suggest in case of a friends' need for impression making?	%0	%100
Which impression technique do you prefer from point of time involved with impression procedure?	%0	%100
Which impression technique do you prefer from point of feeling taste/smell or voice/heat during impression procedure?	%0	%100
Which impression technique do you prefer from point of the size of the intraoral scanner/impression tray used in your mouth during impression procedure?	%0	%100
Which impression technique do you prefer from point of having tooth/gingival sensitivity during impression procedure?	%0	%100
Which impression technique do you prefer from point of having difficulty in breathing during impression procedure?	%0	%100
Which impression technique do you prefer from point of having gagging reflex during impression procedure?	%0	%100

Figure 55 A 9-item comparative questionnaire from Yuzbasioglu *et al.*, (2014).

A recent paper by Grunheid *et al.*, (2014) was in contrast to these results finding 73.3% of patients preferred alginate impressions as they were 'easier' or 'faster' than an intra-oral scan. Only 26.6% showed a preference for the intra-oral scan stating it was 'more comfortable' than an impression. The differing results to this study may be due to the 'routine' patients having a lower burden of care and are unlikely to have had multiple impressions previously. The scanner used (Lava COS; 3M ESPE, Minneapolis, USA) requires a titanium dioxide powder to be applied prior to scanning which may have had a confounding impact on the patients reflections of their experience.

The findings of the participant questionnaires in this study were reflected by the feedback from the parent/carers regarding their child's experiences of the impressions and intra-oral scanning. The parents/carers preferred their child's experience of 3D scanning when compared to the routine impressions ($p=0.003$) and expressed a preference for their perception for the amount of time taken for the intra-oral scan in comparison to the impression ($p=0.03$).

The second null hypothesis was therefore rejected as patient and parent acceptability was greater for the intra-oral scans compared to routine dental impressions.

The findings regarding the time taken are again in keeping with those of Yuzbasioglu *et al.*, (2014).

The authors found digital impression taking to be more time efficient than the conventional

impression technique and patient comfort was higher. Overall they reported that the subjects preferred the digital impression technique to a statistically significant level ($p < 0.001$).

Lee and Gallucci (2013), also found digital impressions (Cadent iTero, Carstadt, USA) resulted in a more efficient technique than conventional impressions when assessed by total treatment time ($P < 0.001$). The scans and impressions were undertaken by 2nd year undergraduate dental students on a customized model representing a single dental implant. It was highlighted that an advantage of the 3D scanning technique was that the ability to rescan any areas that needed further imaging was time saving as if this occurs with a routine an impression a full impression re-take is required.

Grunheid *et al.*, (2014), also found less favourable results in relation to the time taken to perform intra-oral scans versus routine alginate impressions. The time taken for impressions was significantly shorter than intra-oral scans ($p < 0.0001$) but when processing times were included there was no difference ($p = 0.0649$). The time taken to carry out intra-oral scanning decreased with operator experience with each successive scan taking 12 seconds less but this was not statistically significant ($p = 0.2944$). The difference in scanning times could be attributable to the intra-oral scanning system (Lava COS (3M ESPE, Minneapolis, USA) used by the authors which requires excellent moisture control and the application of a titanium dioxide powder. The scanner used in this study did not require strict moisture isolation and did not require a powder.

6.2 Statistical Methodology

The data from the examiner scoring for the plaster, indirect and direct 3D digital models was a cumulative categorical score from a 40 point categorical quasi-continuous scale for MHB and a 5 point ordinal categorical scale for GOSLON Yardstick. The questionnaire data was categorical in nature. The analysis of the data is discussed.

6.2.1 Assessment of examiner reliability

Reliability has been defined as “measurements of individuals on different occasions, or by different observers, or by similar or parallel tests, produce the same or similar results” (Streiner and Norman 1995).

Scoring for each medium (plaster, indirect and direct digital models) was carried out by three examiners, to determine the generalisability of the results, on two separate occasions to allow reliability to be assessed.

‘A high degree of internal consistency is desirable, because it speaks directly to the ability of the clinician or the researcher to interpret the composite score as a reflection of the test’s items’ (Streiner 2003). Cronbach’s alpha is the most widely used index of the reliability of a scale (Peterson 1994).

The ICC reliability (Cronbach’s alpha model) has been successfully used to assess the internal consistency in previous studies using categorical surgical outcome measures including GOSLON Yardstick (Dobbyn *et al.*, 2012, Nollet *et al.*, 2005) and the Five-year-old index (Bongaarts *et al.*, 2004). A reliability coefficient over 0.90 has been generally accepted as sufficient agreement by several authors for clinical application (Bland and Altman 1997, Kaplan 1982, Nunnally 1978) and was therefore adopted for this study.

Previous research has investigated the reliability of GOSLON Yardstick scoring using plaster models of patients with UCLP (Dobbyn *et al.*, 2012, Nollet *et al.*, 2005). Their findings (Table 17) were of similar reliability coefficients than the results from this study.

Authors	Examiners	Mean Reliability Coefficient
(Nollet <i>et al.</i> , 2004)	4	0.83
(Dobbyn <i>et al.</i> , 2012)	2	0.99

Table 17 Mean reliability coefficients for GOSLON from the literature.

6.2.2 Questionnaire analysis

Statistical analysis using the Wilcoxon Signed-Rank Test (Wilcoxon 1946), with $p=0.05$ as the threshold for statistical significance, was performed to evaluate the differences in participants and parent/carer feedback regarding the routine dental impressions and intra-oral scans. This was appropriate as the data was paired, the pairs were chosen randomly and independently and were from an ordinal scale.

6.3 Indices

The literature search (Table 14 and Table 15) identified that the index most frequently used for the assessment of UCLP outcomes from digital mediums since its publication has been the GOSLON index (3 studies) closely followed by the MHB and 5 year olds indices (both 2 studies). Asquith and McIntyre (2012) were the only authors to apply more than one index to both the digital and plaster model mediums. The inclusion of more than one surgical outcome index helps to demonstrate the versatility of a potential new technology for recording the occlusion and for this reason, both the GOSLON and MHB indices were used in the study reported here.

6.3 Sample Size

As no previous research has used direct 3D scans to undertake surgical outcome scoring there was a lack of data available for a power calculation to be performed. The following strategies were therefore adopted to determine the appropriate sample size:

- A. Sample sizes range from 20 to 70 (Table 15) within the previous literature. Formal sample size calculations were reported in the studies by Chawla *et al.*, (2013) and McAuliffe *et al.*, (2010) as follows:

The sample size of 45 was chosen because for reliability and reproducibility tests, a number greater than 40 has been recommended (Chawla *et al.*, 2013).

- B. Correspondence with one of the co-authors of a study on a similar theme using indirect 3D digital study models for surgical outcome scoring in UCLP (Asquith and McIntyre, 2012) confirmed that a power calculation was performed although this was not included in the published paper:

A sample size of 34 was determined to have a power of 80% to identify a clinically important difference of >1 GOSLON categorical point $p < 0.05$ between 2 model formats.

- C. Springate's work (Springate 2012) on the effect of sample size outlines that the distribution about the mean rapidly becomes narrow upwards of 30 samples (and to a lesser degree with over 100 samples).
- D. The above data were discussed with a statistician and it was determined that the study should recruit a minimum of 30 participants. A total of 60 patients were contacted to allow a non-attendance rate of 50%. In total, there were 46 participants, which was greater than the minimum acceptable number with a power of 76.5%.

The minimum number of participant questionnaires was determined based on a clinical difference of 1 categorical point (standard deviation = 1.4), 80% power and $\alpha = 0.05$. This indicated that a sample of 16 participants would be required to complete the questionnaire.

6.4 Data Collection

Patients were recruited prospectively to take part in the study for the following reasons.

All of the previous published literature regarding surgical outcome scoring in OFC was carried out on archived plaster study models and photographs. Retrospective records are at risk of being incomplete or damaged and it is not possible to obtain patient feedback without memory bias. There is potential for selection bias if records are not chosen randomly or consecutively. Prospective data collection although reliant on participants attending clinics allows concurrent records and feedback to be collected. As a result, assessment of dental arch relationships and patient/carer perception of impressions and intra-oral scans using a prospective cohort of patients with UCLP from one centre would minimise these sources of bias and overcomes some of the drawbacks of earlier investigations outlined in Table 14 and Table 15.

6.5 Patient Group

Details of the participants and their recruitment are discussed:

6.5.1 Participant Residence

The study population was from the most populous part of Scotland (core population 1.2 million) served by the NHS Greater Glasgow and Clyde health board region as this is the largest population of patients with clefts in Scotland.

As the 3D scanner was only on loan for a short period of time it was felt that the sample size requirement would be met from this patient cohort within the limited timeframe. Ideally patients would have been recruited from across Scotland but this was not possible due to the logistics of the loan of the scanner.

6.5.2 Inclusion and Exclusion Criteria

In the literature the most commonly analysed cleft type when assessing different records for surgical outcome indices is UCLP and only one study (Leenarts *et al.*, 2012) investigated BLCP. Non-syndromic patients with UCLP were chosen as this presentation is the most representative of the spectrum of surgical and non-surgical interventions in cleft care. It is therefore anticipated that the

results are generalisable to all other cleft sub-phenotypes and indeed to orthodontics in general. The GOSLON Yardstick is not as versatile as MHB in that it is not designed to be used for non-UCLP patients. A comparison of the two indices is outlined Table 18.

As GOSLON is the most commonly used index we wanted to assess its reliability in each model medium but this limited recruitment to subject with UCLP. It was key to include MHB in the study as it has recently been recommended as the standard for the measurement of outcomes for patients with CLP (Altalibi *et al.*, 2013). The ability to successfully carry out scoring using both indices adds further evidence for the argument to change clinical practice from routine impression taking to intra-oral scanning.

	GOSLON	MHB
Cleft Type	UCLP	Any
Age of use	Late mixed dentition/early permanent dentition only	Any
Scale used	5 point scale	40 point ordinal quasi-continuous scale
Scoring	Categorical (1-5)	Cumulative score from continuous numerical scale (-30 to +10)
Calibration required	Yes (reference models also required)	No
Examiner	Experience in cleft care required	Any member of dental team
Potential for automated digital scoring	No – requires examiner experience	Yes

Table 18 Comparison of GOLSON Yardstick and MHB Indices.

The age range of 5-21 years was proposed to maximise subject numbers. Even with OFC being the most common craniofacial anomaly and recruiting from the largest cohort of UCLP patients within a single Scottish health board overall potential recruitment numbers were limited.

The selected age range included the groups of patients who routinely undergo dental impressions for audit records. The potential to remove the burden of care of dental impressions for these groups is the most important. This group was selected in order to provide an unbiased opinion of the experiences of impressions and 3D intra-oral scanning. To complement the views of children, the views of their parent/carer were also sought.

6.5.3 Participant Recruitment

Patients were recruited consecutively from the CLEFTSiS record registry. Of the 60 potential participants contacted 46 attended. Although many of the non-participants had incorrect contact details, all effort were undertaken to minimise participation bias. This consecutive sample of patients from a single cleft centre also minimised selection bias as these subjects would have experienced similar audit records previously, including impressions taken by the same or similar clinicians. Although not all potential subjects who were contacted eventually volunteered, only a few participants refused to have an impression taken, which minimised the impact of non-participation on the data.

Patients across the age range had been identified and sent information regarding the study. The youngest participants recruited were 9 years of age and the oldest were at the upper limit of the age range of 21 (Figure 43). Ideally some younger patients would have taken part but the study relied on participant attendance. Despite the fact that there were few patients under the age of 10 (for which the GOLSON Yardstick was described) it was deemed acceptable to use the GOSLON Yardstick for all those in this study.

6.6 Methodology

Strategies were undertaken as part of the materials and method to minimise bias / confounding.

Each stage is discussed in turn.

6.6.1 Patient Information Sheets (PIS)

Once identified as a potential participant from the CLEFTSiS database a covering letter, parent/carer information sheet and a PIS were sent out by postal mail. The three age groups for the PIS were age 5 (appendix I), 6-10 (appendix III) , 11-15(appendix IV) and 16-21 (appendix V). The detail and explanation of the study increased in depth with each age group. All material sent to potential participants was approved by the co-sponsors and ethics committee.

By sending the information to the potential participants in advance of their appointment would allow them to consider taking part prior to attending the data collection clinic. It was confirmed during the consent process if that patient had received the information prior to taking part in the study.

6.6.2 Consent / Assent

Written consent was obtained from all participants prior to data collection. A consent form (appendix IX) and a parent/carer consent form (appendix XI) were approved by the co-sponsors and ethics committee. An assent form (appendix X) was also available if any participants aged 5 attended. This was done to allow the younger patients to agree to participate in the research study when consent is not appropriate for reasons of competence. All consent forms were counter signed by a single member of the research team (EC).

6.6.3 Impressions

To eliminate any variations in impression taking technique and potential negativity regarding impressions, a single operator (TG) performed all the impressions and occlusal wax bites. The same brand of impression trays and impression material were used throughout. A variety of dental nurses

were allocated to the clinic during the data collection period. To remove and differences in mixing of the impression material an automated mixer was used (Figure 27). All the participants had impressions undertaken first and then went on to have an intra-oral 3D scan.

6.6.4 Intraoral Scanning

A single operator (EC) underwent an intensive 1 day of training in the use of the Trios (www.3shape.com) intra-oral scanner. The same operator undertook the intraoral scanning of all the participants to remove discrepancies due to operator experience or technique. It was noted that as the data collection period progressed operator speed and proficiency with increased experience improved. The time taken for each scan was not recorded. This could potentially be measured in future studies of a similar nature.

It was found by the operator (EC) that the scanner tip was quite large in the younger participants' mouths. This allowed the shorter mixed dentition arches to be captured swiftly with the scanner but may have felt bulky to the participant. It is likely that with future developments in 3D scanning technology that scanner tips will become smaller in size.

6.6.5 Indirect Scanning

All of the plaster models were scanned by the R700 3D model scanner (www.3shape.com) using the same standard technique. Once each individual arch had been scanned the models were articulated, placed into a mounting jig and orientated correctly within the scanner. The same jig was used throughout to minimise bias.

6.6.6 Questionnaire

A closed-ended rating scale questionnaire (appendix VII) was created to obtain feedback on the participants' experiences on having routine dental impression and the intra-oral scan.

No questionnaire had previously been published in the literature with the aim of gathering this information from patients with OFC. Although the questionnaire itself was not specifically validated

for this study, the format of the questionnaire was based on the previously validated patient assessment questionnaires given to patients of Vocational Dental Practitioners (Hurst *et al.*, 2004). The questionnaire was noted to have face validity.

The questions asked were kept very simple as the same questionnaire was to be completed for all age ranges. The response options were also very straight forward 'Very Good' (1), 'Good' (2), OK (3), Bad (4) to 'Very Bad' (5). The option of 'don't know (X)' was also included for any participants who weren't sure or did not want to comment.

The participants completing the questionnaire are highly likely to have undergone routine impressions as part of their previous cleft audit records. An element of their feedback may have been influenced by previous experiences of dental impressions at a younger age. It was emphasised verbally to all of the patients to reflect on their experiences from the data collection clinic, but bias from prior memories could not be fully eliminated. On reflection, a yes/no question could have been included in the questionnaire asking if the patient had previously had impressions and if yes, how many times. This would have allowed further data analysis to be undertaken to evaluate if any differences existed between those with prior experience of impressions and those with no experience of dental impressions.

Feedback was also sought from an accompanying parent/carer (appendix VIII) as their input was also very valuable in the assessment of the perception of impressions and intra-oral scanning.

6.6.7 Model Scoring

All mediums of study models were anonymised for scoring and had no associated patient information. Each format of model was scored on two occasions at least one month apart to eliminate memory bias. Scoring was carried out by each examiner individually to exclude and conferring or discussion. The plaster GOSLON Yardstick reference models were available at each scoring session.

It was not possible to blind the examiners to the medium of the models. The appearance of the bases of the direct and indirect 3D models differed slightly as the direct cases were perfectly linear, whereas the indirect models showed any surface irregularity of the scanned plaster surface. These differences were not thought to influence scoring.

None of the examiners use 3D digital study models as part of their routine clinical practice. This eliminated any advantages that one examiner may have over another regarding experience of working with the new study model mediums of direct and indirect 3D digital study models.

6.8 Alternative Methods

Alternative methods to answer the research question could have included taking impressions and intra-oral scans for non OFC patients. This would have vastly increased the cohort of patients available for recruitment. Non-cleft patients are more likely to have a lower burden of care unless they have another dental anomaly requiring multiple impressions to be taken. It would have been possible to obtain patient feedback from these patients and carry out measurements from the plaster and digital models but it would be inappropriate to carry out GOSLON Yardstick and MHB scoring. Furthermore their lack of previous experience of impressions would potentially influence the results.

Other patients groups requiring multiple impressions could have been studied, such as patients requiring orthognathic surgery or joint orthodontic and restorative treatment for hypodontia. It is currently unlikely to be able to eliminate impressions for these groups of patients at present as plaster models are required for the fabrication of orthodontic appliances and surgical planning. With the advent of 3D printing it may be possible in the future to print accurate study models from intra-oral scanning.

6. 9 Review of Study

The strengths and weaknesses of the study are outlined.

6. 9.1 Strengths of the Study

This was an original study, at the time there was no published literature on undertaking surgical outcome scoring from direct intra-oral 3D digital scans.

The study was adequately powered (76.5%) due to the 76% attendance rate at the data collection clinics surpassing the sample size requirement of 30 participants for impression taking / intra-oral 3D scanning and 16 for questionnaire completion.

The prospective nature of the data collection allowed the addition of a participant and parent/carer questionnaire. Positive feedback regarding the participants' experiences of undergoing intra-oral scanning in comparison to the current practice of taking dental impressions helped validate the recommendation of implementing the new technology onto cleft audit clinics.

As feedback from patients who withdrew from having impressions was not included, this reduced bias. The inclusion of a cohort of patients of a single cleft sub-phenotype from a single centre, and with impressions and intra-oral scans being recorded by single operators, all helped to ensure homogeneity of the data minimising bias.

6.9.2 Weaknesses

Only participants aged 9 years or older attended the data collection clinics reducing the generalisability of the findings.

Due to limitations on the loan period of the intra-oral scanner it was only possible to collect data from patients from area single cleft centre.

Patients and their parents/carers were asked to reflect on their experience of the time taken for routine impressions and the intra-oral scan. The actual time taken was not recorded which would have allowed analysis of any correlation between patient perception and the actual time taken.

The exclusion of participants over the age of 21 may reduce the generalisability of the findings.

Recruitment of older participants may have proved challenging as they are not routinely recalled for audit data collection and there may not be up-to-date contact details on the CLEFTSiS database if they have moved away from their childhood home.

Similarly the exclusion of under 5 year olds may have adversely affected the generalisability of the findings. It would have been worthwhile to obtain their feedback regarding the scanning experience and the feasibility of undertaking the procedure. Feedback from their parent/carer would potentially be more reliable than the participants due to their younger age. It would have not been appropriate to give a GOSLON Yardstick score to models from younger patients.

The questionnaire used was not validated but a similar structure was adopted from a validated dental questionnaire used on a national basis.

All patients underwent routine impressions first then intra-oral 3D scan second. It may have been of benefit to randomise patients into 2 parallel groups: group 1 having impression then scan and group 2 the reverse. Similar randomisation was carried out by (Grunheid *et al.*, 2014). This could help reduce any bias that the order of undergoing each procedure may have on the patients' experience.

Other limitations were that UCLP was the only cleft sub-phenotype recruited and GOSLON and MHB were the only indices used in the study. It would have been ideal to include other cleft sub-phenotypes and other indices, but these would have resulted in heterogeneity, which could have caused confounding of the results.

6.10 Implications for clinical practice/recommendations for future research

- Intra-oral scans have the potential to replace impressions for clinical audit and the assessment of surgical outcomes for subjects with UCLP.
- Archiving current UCLP plaster model records using indirect 3D digital study models would reduce demands on storage space and would create a digital database of digital models readily available for inter-centre/international audit and research. Future audit data collection with an intra-oral scanner would allow the records to be stored digitally on a prospective basis.
- The results from this study could be used to calculate sample sizes for future research.
- Future research could be expanded to include other OFC sub-phenotypes and their associated indices.
- Extending the research team to include other members of the dental team such as nurses or therapists trained to use the scanner to assess whether the reliability of the scans is affected by operator experience. This could also be applied to MHB scoring of direct digital models as no clinical experience in cleft care is required to undertake the scoring.
- The focused recruitment of younger participants would allow validation of intra-oral scanning for audit data collection for this cohort of patients. This could be extended to the scanning of babies with OFC prior to their primary surgery.
- The development of an algorithm within the 3D viewing software to automatically calculate an MHB score would remove the majority of error and subjectivity from the scoring.

CHAPTER SEVEN: CONCLUSIONS

- Reliability of GOSLON and MHB scoring using intra-oral three dimensional (3D) scans was superior to both plaster and indirect 3D digital models.
- Subjects with UCLP and their parent/carer preferred the experience of the intra-oral 3D scan in comparison to routine dental impressions.
- This study supports the replacement of conventional impressions with intra-oral 3D scans in longitudinal evaluations of the outcomes of cleft care.

CHAPTER EIGHT: APPENDICES



(Name)

(date)

(Address)

Dear Parent/Guardian of (name),

New Scanning Device for Checking Teeth After Treatment for Cleft Lip And Palate

We are a team of Orthodontist from the Glasgow Dental Hospital, Dundee Dental Hospital and the University of Dundee. We are very interested in improving treatments for children with cleft lip and palate.

Your child is due to attend the Cleft Clinic at the Glasgow Dental Hospital. We would like to invite your child to take part in a research study when they attend. The research aims to see if we can use a 3D (three dimensional) scanner to create study models of your child's teeth. We hope that in the future the 3-D scanners will replace the need for dental impressions which is the current practice.

Please find enclosed an information sheet for you and your child to read before your appointment. Taking part in the study is voluntary. If you or your child has any questions please do not hesitate to contact us or if you would like independent advice on taking part in research contact details are provided on the information sheet.

Yours Sincerely,

Dr Toby Gillgrass, Consultant Orthodontist, Glasgow Dental Hospital

Professor Peter Mossey, Consultant Orthodontist, Dundee Dental Hospital

Dr Grant McIntyre, Consultant Orthodontist, Dundee Dental Hospital

Miss Elinor Chalmers, Orthodontic Specialty Trainee, Dundee Dental Hospital



Patient Information Sheet for participants aged 5

New Scanning Device for Checking Teeth After Treatment for Cleft Lip And Palate

Study Investigators: Miss E Chalmers, Prof P Mossey, Dr G McIntyre, Dr T Gillgrass

Please show this leaflet to your child prior to attending the Cleft Clinic.

Who can take part?

We would like boys and girls who had treatment for cleft lip and palate to help us.

Can I take part?

Yes you are the right age to join the study.

Do I have to take part?

You don't have to take part if you don't want to.

Is it safe for me to take part?

Yes the study has been checked to make sure it is ok.

What do I have to do in the study?

You have to have impressions taken of your teeth so we can remember what your teeth look like. We also would like to use hand held scanner which scans your teeth so we can look at them on a computer. You will be asked to complete a short questionnaire.



An impression

Appendix II



The 3D scanner- computer screen and wand.



The wand that scans your teeth.

What should I do next?

You should talk to the person who is looking after you about taking part in the study. You need to decide with them if you are going to take part.

Thank you for reading this – please ask any questions if you need to.



Patient Information Sheet for participants aged 6-10

New Scanning Device for Checking Teeth After Treatment for Cleft Lip And Palate

Study Investigators: Miss E Chalmers, Prof P Mossey, Dr G McIntyre, Dr T Gillgrass

What is research? Why is this project being done?

Research is a way we try to find out the answers to questions. We are asking if you would join in a research project to find the answer to the question: can we use a 3D scanning device to check teeth after treatment for cleft lip and palate?

Why have I been asked to take part?

You have been invited to join our study because you have been treated for cleft palate and or lip. Fifty children with cleft palate and or lip will be studied in this project.

Did anyone else check the study is OK to do?

Before any research is allowed to happen, it has to be checked by a group of people called a Research Ethics Committee. They make sure that the research is fair. Your project has been checked by the West of Scotland Research Ethics Committee.

Do I have to take part?

You do not have to take part in the research if you do not want to. If you decide not to take part this will not stop you getting your teeth cared for.

What will happen to me if I take part in the research?

- You will attend your routine Cleft Clinic appointment.
- One of the research team will explain this information leaflet to you. You will have the chance to ask questions.
- If you would like to take part you will be asked to sign a form that says you would like to take part in the research.
- You will have a routine impression taken of your teeth.
- You will have a 3D scan taken of your teeth. The wand of the scanner will be placed in your mouth and it will send the pictures of your teeth to a computer. There is a picture of the scanner in the leaflet for you to see.
- After your appointment you will be asked to fill out a short questionnaire about your experience of having an impression and a 3D scan taken.

Appendix III



- You will be involved in this study for this appointment only, which will last about 45 minutes.



What the 3D scanner looks like.

What are the possible benefits of taking part?

We cannot promise the study will help you but the information we get might help young people with cleft lip and palate by replacing routine dental impressions with 3D scans.

What if something goes wrong during the project?

If anything goes wrong during the project your parent or carer can speak to one of the research team and they will be able to make a complaint to the NHS.

Will my medical details be kept private if I take part? Will anyone else know I'm doing this?

We will keep your information in confidence. This means we will only tell those who have a need or right to know. Wherever possible, we will only send out information that has your name and address removed.

What if I don't want to do the research anymore?

If at any time you don't want to do the research anymore, just tell your parents, dentist or dental nurse. They will not be cross with you.

Thank you for reading this – please ask any questions if you need to



Patient Information Sheet for participants aged 11-15

New Scanning Device for Checking Teeth After Treatment for Cleft Lip And Palate

Study Investigators: Miss E Chalmers, Prof P Mossey, Dr G McIntyre, Dr T Gillgrass

We are asking if you would join in a research project to find the answer to the question: can we use a 3D scanning device to check teeth after treatment for cleft lip and palate?

Before you decide if you want to join in, it's important to understand why the research is being done and what it will involve for you. So please consider this leaflet carefully. Talk to your family, friends, dentist or orthodontist if you want to.

Part 1

Why are we doing this research?

We want to find out if using a 3D scanner to check teeth after treatment for cleft lip and palate is as reliable as taking dental impressions of teeth.

What is a 3D scanner?

A 3D scanner is a computer with a scanner wand attached. The wand is placed inside your mouth and it scans your teeth. The scans of your teeth are sent to the computer and create a 3D model of your teeth on the screen. The model of your teeth can be saved on the computer to allow measurements to be taken to check the teeth.



Why have I been invited to take part?

Appendix IV



You have been invited to join our study because you have been treated for cleft palate and or lip. Fifty children with cleft palate and or lip will be studied in this project. This is the first time the 3D scanner has been used to check teeth after treatment for cleft lip and palate.

Do I have to take part?

No. It is up to you. We will ask you for your consent and then ask if you would sign a form. We will give you a copy of this information sheet and your signed form to keep. You are free to stop taking part at any time during the research without giving a reason. If you decide to stop, this will not affect the care you receive.

What will happen to me if I take part?

- You will attend your routine Cleft Clinic appointment.
- One of the research team will explain this information leaflet to you. You will have the chance to ask questions.
- If you would like to take part you will be asked to sign a consent form.
- You will have a routine impression taken of your teeth.
- You will have a 3D scan taken of your teeth.
- After your appointment you will be asked to fill out a short questionnaire about your experience of having an impression and a 3D scan taken.
- You will be involved in this study for this appointment only, which will last about 45 minutes.

What are the possible benefits of taking part?

We cannot promise the study will help you but the information we get might help young people with cleft lip and palate by replacing routine dental impressions with 3D scans.

Thank you for reading so far – if you are still interested, please go to Part 2:

Contact us:

If you have any questions about being involved in this study please contact:

Appendix IV



Dr Grant McIntyre, Email: grant.mcintyre@nhs.net, Telephone: 01382635964

If you have any questions about being part of a research project and would like to ask someone who is not directly involved with this study, please email or ask whoever looks after you to email:

Dr F Borrie, Clinical Lecturer, University of Dundee Dental Hospital and School

f.borrie@dundee.ac.uk

Part 2

What if there is a problem?

In the event that something goes wrong and you are harmed during the study there are no special compensation arrangements. If you are harmed and this is due to someone's negligence then you may have grounds for a legal action for compensation against the University of Dundee or NHS Tayside but you may have to pay your legal costs. The normal National Health Service complaints mechanisms will still be available to you.

If you have a complaint about your child's participation in the study you should first talk to a researcher involved in your child's care. You can ask to speak to a senior member of the research team or the Complaints Officer for NHS Greater Glasgow and Clyde

Complaints Office

Glasgow Royal Infirmary

Castle Street

Glasgow G4 0SF

Phone: 0141 211 5112

Further information on your Health Rights please visit the following website:

<http://www.hris.org.uk/>

Will anyone else know I'm doing this?

We will keep your information in confidence. This means we will only tell those who have a need or right to know. Wherever possible, we will only send out information that has your name and address removed.

Appendix IV



Who is organising and funding the research?

The study is sponsored by the University of Dundee and NHS Tayside and funded by the Scottish Cleft Lip and Palate Association.

Who has reviewed the study?

Before any research goes ahead it has to be checked by a Research Ethics Committee. They make sure that the research is fair. Your project has been checked by the West of Scotland Research Ethics Committee.

Thank you for reading this – please ask any questions if you need to.



Patient Information Sheet for participants aged 16-21

New Scanning Device for Checking Teeth After Treatment for Cleft Lip And Palate

Study Investigators: Miss E Chalmers, Prof P Mossey, Dr G McIntyre, Dr T Gillgrass

Contact us:

If you have any questions about being involved in this study please contact:

Dr Grant McIntyre – Email address: grant.mcintyre@nhs.net Telephone: 01382 635964

If you have any questions about being part of a research project and would like to ask someone who is not directly involved with this study, please email or ask whoever looks after you to email: Dr Felicity Borrie, Clinical Lecturer, University of Dundee Dental Hospital and School Email address: f.borrie@dundee.ac.uk

We are asking if you would join in a research project to find the answer to the question: can we use a 3D scanning device to check teeth after treatment for cleft lip and palate?

Before you decide if you want to join in, it's important to understand why the research is being done and what it will involve for you. So please consider this leaflet carefully. Talk to your family, friends, dentist or orthodontist if you want to.

Part 1

Why are we doing this research?

We want to find out if using a 3D scanner to check teeth after treatment for cleft lip and palate is as reliable as taking dental impressions of teeth. Study models are taken at routine Cleft Clinics to help monitor your treatment progress and for audit and research purposes.

What is a 3D scanner?

A 3D scanner is a computer with a scanner wand attached. The wand is placed inside your mouth and it scans your teeth. The scans of your teeth are sent to the computer and create a 3D model of your teeth on the screen. The model of your teeth can be saved on the computer to allow measurements to be taken to check the teeth.

Why have I been invited to take part?

You have been invited to join our study because you have been treated for cleft palate and or lip. Fifty children and young people with cleft palate and or lip will be studied in this project. This is the first time the 3D scanner has been used to check teeth after treatment for cleft lip and palate.



Do I have to take part?

No. It is up to you. We will ask you for your consent and then ask if you would sign a form. We will give you a copy of this information sheet and your signed form to keep. You are free to stop taking part at any time during the research without giving a reason. If you decide to stop, this will not affect the care you receive.

What will happen to me if I take part?

- You will attend your Cleft Clinic appointment.
- One of the research team will explain this information leaflet to you. You will have the chance to ask questions.
- If you would like to take part you will be asked to sign a consent form.
- You will have a routine impression taken of your teeth.
- You will have a 3D scan taken of your teeth.
- After your appointment you will be asked to fill out a short questionnaire about your experience of having an impression and a 3D scan taken.
- You will be involved in this study for this appointment only, which will last about 45 minutes.

What are the possible benefits of taking part?

We cannot promise the study will help you but the information we get might help young people with cleft lip and palate by replacing routine dental impressions with 3D scans.

Thank you for reading so far – if you are still interested, please go to Part 2:

Part 2

What if there is a problem?

In the event that something goes wrong and you are harmed during the study there are no special compensation arrangements. If you are harmed and this is due to someone's negligence then you may have grounds for a legal action for compensation against the University of Dundee or NHS Tayside but you may have to pay your legal costs. The normal National Health Service complaints mechanisms will still be available to you.

Appendix V



If you have a complaint, please contact:

Complaints Office

Glasgow Royal Infirmary

Castle Street

Glasgow G4 0SF

Phone: 0141 211 5112

Further information on your Health Rights please visit the following website:

<http://www.hris.org.uk/>

Will anyone else know I'm doing this?

We will keep your information in confidence. This means we will only tell those who have a need or right to know. Wherever possible, we will only send out information that has your name and address removed.

Who is organising and funding the research?

The study is sponsored by the University of Dundee and NHS Tayside and funded by the Scottish Cleft Lip and Palate Association.

Who has reviewed the study?

Before any research goes ahead it has to be checked by a Research Ethics Committee. They make sure that the research is fair. Your project has been checked by the West of Scotland Research Ethics Committee.

Thank you for reading this – please ask any questions if you need to.



Information Sheet for Parent/Carer

Study: New Scanning Device for Checking Teeth After Treatment for Cleft Lip And Palate

Study Investigators: Miss E Chalmers, Prof P Mossey, Dr G McIntyre, Dr T Gillgrass

We would like to invite you to take part in our research study. This study is part of Miss E Chalmers' University of Dundee Masters by research project. Before you decide we would like you to understand why the research is being done and what it would involve for your child. One of our team will go through the information sheet with you and answer any questions you have. We'd suggest this should take about 10 minutes

Talk to others about the study if you wish.

(Part 1 tells you the purpose of this study and what will happen to you if you take part. Part 2 gives you more detailed information about the conduct of the study).

Ask us if there is anything that is not clear.

Part 1

What is the purpose of the study?

This study is about collecting dental study models and three dimensional (3-D) scans of patients with cleft lip and palate. Dental study models are casts made of plaster and are normally created by taking impressions of the upper and lower teeth. Study models are taken at routine Cleft Clinics to help monitor your child's progress and for audit and research purposes. An intra-oral three dimensional scanner has been created that can scan the teeth without taking an impression. We are asking you to give consent for your child to take part in a study about using this new technique to scan their mouth.

Why has my child I been invited?

Your child has been identified from the National Managed Clinical Network for Cleft Service in Scotland (CLEFTSiS) data base as having a cleft lip and palate and is the correct age to take part in the study.

Does my child have to take part?

It is up to you and your child to decide to join the study. We will describe the study and go through this information sheet. If you agree to take part, we will then ask you to sign a consent form and your child to sign an assent form. You are free to withdraw your child at any time, without giving a reason. This would not affect the standard of care you receive.



What will happen to my child if they take part?

Your child will attend their routine appointment at the Cleft Clinic. They will be involved in this study for this single appointment only, which will last approximately 45 minutes. The study models and 3D scans of your child teeth will be analysed to see if using the 3D scanner is a reliable method of checking teeth after treatment for cleft lip and palate.

What will my child have to do?

You and your child will have the information sheet explained to you. If you both agree to take part in the study you will sign a consent form and your child will sign an assent form. Routine dental impressions will be taken of your child's upper and lower teeth. They will also have their teeth scanned with the 3D scanner. Afterwards you and your child will be asked to fill out a questionnaire about the experience of having impressions and a 3D scan taken.

Are there any disadvantages or risks to my child taking part?

There is no risk with dental impression or the three dimensional scanner. Both techniques are used by dentists. Having the 3D scan is an additional investigation in addition to the routine dental impressions.

Are there any potential benefits of taking part?

We hope in the future that the three dimensional scanner will replace dental impressions.

Will my child taking part in the study be kept confidential?

Yes. We will follow ethical and legal practice and all information about you will be handled in confidence. The details are included in Part 2.

If the information in Part 1 has interested you and you are considering participation, please read the additional information in Part 2 before making any decision.

Part 2

Who is organising and funding the research?

The study is sponsored by the University of Dundee and NHS Tayside and funded by the Scottish Cleft Lip and Palate Association

Appendix VII



What if there is a problem?

In the event that something goes wrong and your child is harmed during the study there are no special compensation arrangements. If your child is harmed and this is due to someone's negligence then you may have grounds for a legal action for compensation against the University of Dundee or NHS Tayside but you may have to pay your legal costs. The normal National Health Service complaints mechanisms will still be available to you.

If you have a complaint about your child's participation in the study you should first talk to a researcher involved in your child's care. You can ask to speak to a senior member of the research team or the Complaints Officer for NHS Greater Glasgow and Clyde

Complaints Office

Glasgow Royal Infirmary

Castle Street

Glasgow G4 0SF

Phone: 0141 211 5112

Further information on your Health Rights please visit the following website:

<http://www.hris.org.uk/>

Will all the information about my child be kept confidential?

The West of Scotland Research Ethics Committee, which has responsibility for scrutinising all proposals for medical research on humans in NHS Greater Glasgow and Clyde, has examined the proposal and has raised no objections from the point of view of medical ethics. It is a requirement that your child's records in this research, together with any relevant medical records, be made available for scrutiny by monitors from University of Dundee, NHS Tayside and the Regulatory Authorities, whose role is to check that research is properly conducted and the interests of those taking part are adequately protected.

The data we collect about your child will be held against a unique number, which will be issued to them at the start of the study. One member of staff will hold a sheet identifying that this study number belongs to your child, and this information will be kept securely. Your child's stored anonymised data may be used for future non-commercial research.

The study and the information it provides may be presented at conferences and published in journals.

Appendix VII



For further information or help regarding this study please contact:

Chief Investigator:

Dr Grant McIntyre

Email: grant.mcintyre@nhs.net

Telephone: 01382635964

Independent contact point where potential participants can seek general advice about taking part in research:

Dr F Borrie, Clinical Lecturer, University of Dundee Dental Hospital and School

f.borrie@dundee.ac.uk

Thank you for taking the time to read this Information Sheet and for considering your child's taking part in this study

Appendix VII



Patient questionnaire

Please **circle** a number for each question that best shows how you felt about your experiences today.

1= Very Good, **2**= Good, **3**=OK, **4**=Bad, **5**= Very Bad, **X**= I don't know

Having a routine impression of your teeth:

	Very Good	Good	OK	Bad	Very Bad	I Don't Know
The time it took:	1	2	3	4	5	X
How did it feel?	1	2	3	4	5	X

Having a 3-D Scan of your teeth:

	Very Good	Good	OK	Bad	Very Bad	I Don't Know
The time it took:	1	2	3	4	5	X
How did it feel?	1	2	3	4	5	X

Appendix VIII



Parent/Carer Questionnaire

Please **circle** a number for each question that best shows how **you felt** about **your child's** experience today.

1= Very Bad, **2**= Bad, **3**=OK, **4**=Good, **5**= Very Good, **X**= I don't know

Your child's experience of having a **routine dental impression**:

Very Good Good Ok Bad Very Good I Don't Know

The time it took: **1** **2** **3** **4** **5** **X**

How did they cope? **1** **2** **3** **4** **5** **X**

Your child's experience of having a **3-D scan** of their teeth:

Very Good Good Ok Bad Very Good I Don't Know

The time it took: **1** **2** **3** **4** **5** **X**

How did they cope? **1** **2** **3** **4** **5** **X**

Appendix IX

Subject number:



Participant Consent Form

New Scanning Device for Checking Teeth After Treatment for Cleft Lip And Palate

Study Investigators: Miss E Chalmers, Prof P Mossey, Dr G McIntyre, Dr T Gillgrass

For further information or help regarding this study please contact:

Dr Grant McIntyre. Email address: grant.mcintyre@nhs.net Telephone: 01382 635964

Independent contact point where potential participants can seek general advice about taking part in research:

Dr F Borrie, Clinical Lecturer, University of Dundee Dental Hospital and School. Email: f.borrie@dundee.ac.uk

1. I confirm that I have read the information sheet version 2.0 for the above study. ☐
2. I have had a chance to discuss this study and ask questions. ☐
3. I have received satisfactory answers to all of my questions. ☐
4. I have received enough information about the study ☐
5. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected. ☐
6. I understand that sections of my medical notes may be looked at by the research team where it is relevant to my taking part in the research. I give my permission for the research team to have access to my records. ☐
7. I agree to take part in the above study ☐

Name of Patient

Date

Signature

Name of Parent

Date

Signature

Name of Person taking consent

Date

Signature

1 copy to the patient, 1 copy to the researcher, 1 Original for the patients' notes

Appendix X



ASSENT FORM FOR CHILDREN

(To be completed by the child and their parent/guardian)

Project title: New Scanning Device for Checking Teeth After Treatment for Cleft Lip And Palate

Study Investigators: Miss E Chalmers, Prof P Mossey, Dr G McIntyre, Dr T Gillgrass

To be completed by the child (or if unable, the parent on their behalf). Please circle your answers:

Have you read (or had read to you) about this project?	Yes/No
Has somebody else explained this project to you?	Yes/No
Do you understand what this project is about?	Yes/No
Have you asked all the questions you want?	Yes/No
Have you had your questions answered in a way that you understand?	Yes/No
Do you understand that it's OK to stop taking part at any time?	Yes/No
Are you happy to take part?	Yes/No

If any answers are 'no' or you don't want to take part, don't sign your name!

If you do want to take part, you can sign your name below

Your name _____

Signature _____

Date _____

The dentist who explained this project to you needs to sign too:

Print Name _____

Signature _____

Date _____

Appendix XI



Parent/Carer Consent form

Intraoral 3D scanning for assessment of surgical outcome in patients with unilateral cleft lip and palate

Study Investigators: Miss E Chalmers, Prof P Mossey, Dr G McIntyre, Dr T Gillgrass

- ☐ I am giving consent on behalf of _____. My relationship is their parent / carer (please delete as appropriate).
- ☐ I confirm that I have read and understand the participant information leaflet for the above study. I have had the opportunity to consider the information, to ask questions, and have had these questions answered.
- ☐ I understand that my child's participation is voluntary and withdrawal from the study at any time will not affect their orthodontic treatment or legal rights
- ☐ I understand that dental records and the data collected during the study may be looked at by individuals from the University of Dundee or from regulatory authorities where it is relevant to participation in the research. I give permission for these individuals to access my child's records.
- ☐ I consent to 3-D scans and impressions of my child's teeth being taken for scoring by other clinicians.
- ☐ I consent to the images of 3-D scans and models of my child's teeth being used in presentations or publications associated with this study.

_____	_____	_____
Name of participant	Signature of participant	Date
_____	_____	_____
Study investigator	Signature	Date

3 copies: 1 for participant; 1 for researcher file; 1 to be kept in participant's notes

3D Study Model Scoring Round

Examiner:

Subject number:

Goslon Index: Score 1 2 3 4 5

Huddart & Bodenham Score:

Right Buccal Segment

6	E	D	C
-3	-3	-3	-3
-2	-2	-2	-2
-1	-1	-1	-1
0	0	0	0
+1	+1	+1	+1

Sum

Labial Segment

1	1
-3	-3
-2	-2
-1	-1
0	0
+1	+1

Sum

Left Buccal Segment

C	D	E	6
-3	-3	-3	-3
-2	-2	-2	-2
-1	-1	-1	-1
0	0	0	0
+1	+1	+1	+1

Sum

TOTAL SUM

CHAPTER NINE: REFERENCES

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